

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russell Examiner #: 62785 Date: 2-24-2005  
 Art Unit: 1654 Phone Number: 301-571-272-0969 Serial Number: 10/758,717  
 Mail Box and Bldg/Room Location: \_\_\_\_\_ Results Format Preferred (circle): PAPER DISK E-MAIL  
REM 3C18 (mailbox), 3D19 (office)

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

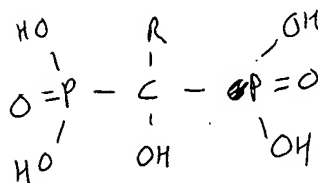
Title of invention: Method of Modifying The Release Profile Of Sustained Release Compositions

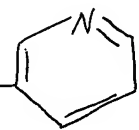
Inventors (please provide full names): J. Dorsch, M. Riley

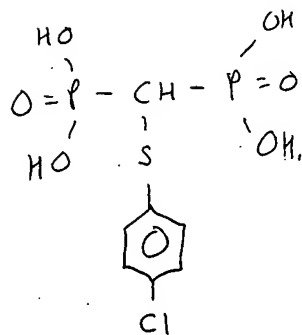
Earliest Priority Filing Date: 1-16-2004

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.


Please search the following structures



where R is  $-\text{CH}_2-$  ,  $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}_2$ ,  
 $-\text{CH}_2-\text{CH}_2-\text{NH}_2$ , or  $-\text{CH}_3$ .



I'm looking for these compounds in pharmaceutical compositions, in particular in combination with biodegradable polymeric carriers, esp. poly(lactide-co-glycolide), in the form of a sustained release/controlled release composition.

Thank you. 

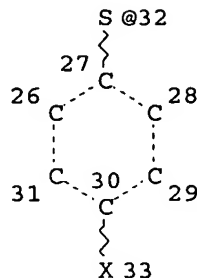
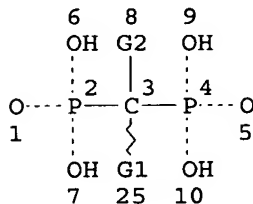
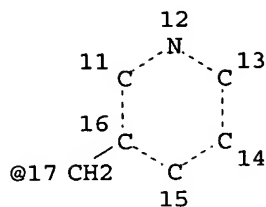
## STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: _____	NA Sequence (#) _____	STN _____
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: _____	Litigation _____	Lexis/Nexis _____
Searcher Prep. / Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep. Time: _____	Patent Family _____	WWW/Internet _____
Online Time _____	Other _____	Other (specify) _____

Russell  
10/758717

=> d l3 que stat;fil medl,biosis,embase,hcapl;s l3  
L1 STR

CH2-CH2-NH2  
@22 23 24



CH2-CH2-CH2-NH2  
@18 19 20 21

VAR G1=17/22/18/ME/32  
VAR G2=H/OH  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE  
L3 595 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 5922 ITERATIONS  
SEARCH TIME: 00.00.01

595 ANSWERS

COST IN U.S. DOLLARS

SINCE FILE  
ENTRY

TOTAL  
SESSION

FULL ESTIMATED COST

164.34

164.55

FILE 'MEDLINE' ENTERED AT 14:18:26 ON 25 MAR 2005

FILE 'BIOSIS' ENTERED AT 14:18:26 ON 25 MAR 2005

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FILE 'EMBASE' ENTERED AT 14:18:26 ON 25 MAR 2005

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FILE 'HCAPLUS' ENTERED AT 14:18:26 ON 25 MAR 2005

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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L4 3749 FILE MEDLINE

L5 1875 FILE BIOSIS

Searched by: Mary Hale 571-272-2507 REM 1D86

L6 9510 FILE EMBASE  
L7 6759 FILE HCAPLUS

TOTAL FOR ALL FILES  
L8 21893 L3

=> s (sustain? or timed or control?) (4a) releas? or polymer? carrier? or poly  
lactide co glycolide or polygalactin 910 or glycolic lactic acid polyester)  
UNMATCHED RIGHT PARENTHESIS 'POLYESTER')  
The number of right parentheses in a query must be equal to the  
number of left parentheses.

=> s (sustain? or timed or control?) (4a) releas? or polymer? carrier? or poly  
lactide co glycolide or polygalactin 910 or glycolic lactic acid polyester  
L9 17682 FILE MEDLINE  
L10 23509 FILE BIOSIS  
L11 29691 FILE EMBASE  
L12 46623 FILE HCAPLUS

TOTAL FOR ALL FILES  
L13 117505 (SUSTAIN? OR TIMED OR CONTROL?) (4A) RELEAS? OR POLYMER? CARRIER?  
OR POLY LACTIDE CO GLYCOLIDE OR POLYGALACTIN 910 OR GLYCOLIC  
LACTIC ACID POLYESTER

=> s l8 and l13  
L14 8 FILE MEDLINE  
L15 1 FILE BIOSIS  
L16 40 FILE EMBASE  
L17 72 FILE HCAPLUS

TOTAL FOR ALL FILES  
L18 121 L8 AND L13

=> s l18 and (pharm? or compos?)  
L19 2 FILE MEDLINE  
L20 1 FILE BIOSIS  
L21 30 FILE EMBASE  
L22 51 FILE HCAPLUS

TOTAL FOR ALL FILES  
L23 84 L18 AND (PHARM? OR COMPOS?)

=> dup rem l23  
PROCESSING COMPLETED FOR L23  
L24 79 DUP REM L23 (5 DUPLICATES REMOVED)

=> d 1-79 ibib abs hitstr; s l8 and (dasch j?/au or riley m?/au)

L24 ANSWER 1 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2005:216714 HCAPLUS  
TITLE: Compositions and methods for delivery of biologically active agents  
INVENTOR(S): Khoo, Shui-mei; Boyd, Benjamin James; Whittaker, Darryl Vanstone; Davey, Gregory Andrew  
PATENT ASSIGNEE(S): DBL Australia Pty. Ltd., Australia  
SOURCE: PCT Int. Appl., 97 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021046	A1	20050310	WO 2004-AU1181	20040901
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: AU 2003-904717 A 20030901  
AU 2003-904719 A 20030901

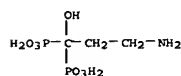
AB The present invention provides methods and compns. for the delivery of a biol. active agent to a biol. system. The compns. include the active agent and a lyotropic phase and release of the active agent to the biol. system is modified by the lyotropic phase. Thus, a formulation contained irinotecan and 2,3-dihydroxypropionic acid 3,7,11,15-tetramethyl hexadecyl ester and water. A sustained release of the drug from the formulation was achieved.

IT INDEXING IN PROGRESS

IT 57248-88-1. Disodium pamidronate  
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compns. for delivery of biol. active agents)

RN 57248-88-1 HCAPLUS

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

L24 ANSWER 2 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2005:119884 HCAPLUS  
DOCUMENT NUMBER: 142:204864  
TITLE: Medical implants coated with porous carbon surfaces carrying drugs  
INVENTOR(S): Rathenow, Joerg; Asgari, Soheil; Ban, Andreas  
PATENT ASSIGNEE(S): Blue Membranes GmbH, Germany  
SOURCE: Ger. Offen., 15 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10333099	A1	20050210	DE 2003-10333099	20030721
DE 202004009061	U1	20040916	DE 2004-202004009061	20040528
WO 2004105826	A2	20041209	WO 2004-EP5785	20040528
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: DE 2003-10324415 A1 20030528  
DE 2003-10333098 A1 20030721  
DE 2003-10333099 A1 20030721

AB The invention concerns a method for the preparation of medical implants with functionalized surfaces involving the steps: (a) preparation of medical implant that is at least partially coated with a carbon-containing layer; (b) activation of the carbon-containing layer by forming a pores on the surface; (c) functionalization of the activated, carbon-containing surface. The carbon-containing layer is composed of pyrolytically prepared carbon, carbon deposited by CVD or PVD process, sputtered carbon, metal carbides, metal carbonitrides, metal oxynitrides, metal oxycarbides or their combinations. The carbon-containing layers are activated by oxidation with air, oxygen, dinitrogen oxide, and oxidizing acids, also at elevated temperature. A reduction process can also be used for activation. Activated surfaces are functionalized by loading one or more drugs, microorganisms or cells onto the surface. Activated surfaces can be sealed in a CVD or CVI (chemical vapor infiltration) process. The implants are prepared from carbon, carbon fibers, ceramics, glass, metals, alloys, artificial bone, stone, minerals. Artificial blood vessels, stents, coronary stents, peripheral stents,

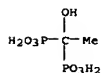
L24 ANSWER 1 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L24 ANSWER 2 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
orthopedic implants, bone and joint prosthesis, artificial heart, heart valves, s.c., and i.m. implants can be activated and functionalized.

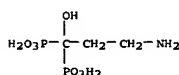
IT 2809-21-4, Etidronic acid 40391-99-9 66376-36-1  
Alendronic acid 89987-06-4, Tiludronic acid 105462-24-6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(medical implants coated with porous carbon surfaces carrying drugs)

RN 2809-21-4 HCAPLUS

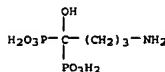
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



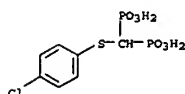
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

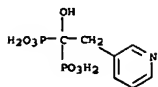


RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [4-(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

Searched by: Mary Hale 571-272-2507 REM 1D86



L24 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2005:119883 HCAPLUS  
 DOCUMENT NUMBER: 142:204863  
 TITLE: Biocompatible coated medical implants with a carbon layer and method for preparation  
 INVENTOR(S): Rathenow, Joerg; Angari, Soheil; Ban, Andreas  
 PATENT ASSIGNEE(S): Blue Membranes GmbH, Germany  
 SOURCE: Ger. Offen., 23 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10333098	A1	20050210	DE 2003-10333098	20030721
DE 202004009060	U1	20040916	DE 2004-202004009060	20040510
WO 2004101017	A2	20041125	WO 2004-EP4985	20040510
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 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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WO 2004105826	A2	20041209	WO 2004-EP5785	20040528

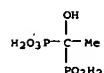
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 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:  
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 DE 2003-10324415 A1 20030528  
 DE 2003-10333098 A1 20030721  
 DE 2003-10333099 A1 20030721

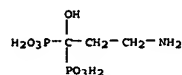
AB The invention concerns a method for the preparation of biocompatible coatings for implants, and medical goods composing the steps (a) coating the medical good at least partially with a polymer film using a coating process; (b) heating the polymer film in an oxygen-free atmosphere at 200-2500 °C to obtain a carbon layer on the medical good. The medical goods are heat resistant; they are prepared from carbon, carbon fibers, ceramics.

L24 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
 glass, metals, alloys, artificial bone, stone, minerals; during heating they are transferred to their thermostable state. Artificial blood vessels, stents, coronary stents, peripheral stents, orthopedic implants, bone and joint prosthesis, artificial heart, heart valves, s.c., and i.m. implants can be coated. Other coating methods, e.g. dipping, spraying, printing can be applied. Several carbon layers with various porosity can be formed; biocompatible, biodegradable, non-biodegradable polymer layers can be placed on top of the carbon layers; drugs can be adsorbed onto the layers.

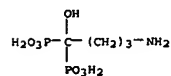
IT 2809-21-4, Etidronic acid 40391-99-9 66376-36-1  
 . Alendronic acid 89987-06-4, Tiludronic acid 105462-24-6  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (biocompatible coated medical implants with a carbon layer and method for preparation)  
 RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 40391-99-9 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

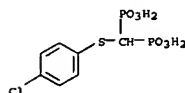


RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

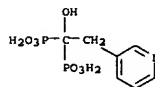


RN 89987-06-4 HCAPLUS  
 CN Phosphonic acid, [(4-chlorophenyl)thio]methylene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 3 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 105462-24-6 HCAPLUS  
 CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 4 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 2005011145 EMBASE  
TITLE: Electrolytic deposition of calcium etidronate drug coating on titanium substrate.  
AUTHOR: Duan K.; Fan Y.; Wang R.  
CORPORATE SOURCE: R. Wang, Department of Materials Engineering, University of British Columbia, 309-6350 Stores Road, Vancouver, BC V6T 124, Canada. rzwang@interchange.ubc.ca  
SOURCE: Journal of Biomedical Materials Research - Part B Applied Biomaterials, (15 Jan 2005) 72/1 (43-51).  
Refs: 31  
ISSN: 0021-9304 CODEN: JBRMGL  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation  
037 Drug Literature Index  
039 Pharmacy

LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Wear debris-induced osteolysis is the major cause of aseptic loosening and failure of hip implants. One of the promising therapeutic interventions

to improve the longevity of hip implants is to administer bisphosphonate drug to inhibit osteoclastic bone resorption. This study aimed at developing new techniques of directly combining bisphosphonate with implants to achieve local delivery and controlled release of the drug. Instead of using soluble sodium salt, we proposed to apply sparingly soluble calcium salt of bisphosphonate as a potential long-term antioleolysis coating on hip implants. Calcium salt of etidronate, a member of the bisphosphonate family of potent osteoclast inhibitors, was used in this pilot study. By adopting the electrolytic deposition (ELD) technique, which was developed for ceramic coatings including calcium phosphates, we demonstrated that a thin layer of calcium bisphosphonate could be deposited onto titanium surface. The drug coating is amorphous as characterized with X-ray diffraction, and has globular morphology under the scanning electron microscope.

Electrospray-ionization mass-spectrometry (ESI-MS) and Fourier-transformed infrared spectroscopy confirmed that the molecular structure of the etidronate (m/z 205, H(3)L(-)), the single dissociated form of parent etidronic acid, denoted

as H(4)L was preserved after the ELD process. In vitro release into a "physiological" buffer solution confirmed that the etidronate concentration

was limited by its low solubility. The etidronate concentration was 8 x 10(-5) M at day 1 and kept relatively stable at approx. 6 x 10(-5) M from day 2 to day 8. The deposition mechanisms of the drug coating and its potential efficacy as an antioleolytic release source were discussed.  
.COPYRG. 2004 Wiley Periodicals, Inc.

L24 ANSWER 5 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN

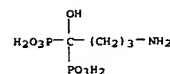
ACCESSION NUMBER: 2004:902159 HCAPLUS  
DOCUMENT NUMBER: 141:370572  
TITLE: Orally disintegrating tablets containing silicified cellulose  
INVENTOR(S): Platteauw, Johannes Jan; Van den Heuvel, Dennie Johan Marijn  
PATENT ASSIGNEE(S): Synthon B.V., Neth.  
SOURCE: PCT Int. Appl., 39 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004:091585	A1	20041028	WO 2004-EP4119	20040416
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004265375	A1	20041230	US 2004-824619	20040415
PRIORITY APPL. INFO.:			US 2003-463027P	P 20030416

AB Silicified microcryst. cellulose is used to provide a tablet with oral disintegration. The tablet contains at least 30% of the silicified microcryst. cellulose and an effective amount of a pharmaceutically active agent. For example, orally disintegrating tablets were prepared containing leflunomide 20.00%, silicified microcryst. cellulose (Prosolvl) 74.50%, low-substituted hydroxypropyl cellulose 5.0%, and Mg stearate 0.54

IT 129318-43-0. Alendronate sodium  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(orally disintegrating tablets containing silicified microcryst. cellulose)

RN 129318-43-0 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI)  
(CA INDEX NAME)



• Na

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L24 ANSWER 5 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)  
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

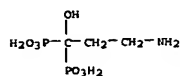
L24 ANSWER 6 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2004:433684 HCAPLUS  
DOCUMENT NUMBER: 140:429037  
TITLE: High viscosity liquid controlled drug delivery system and medical or surgical device  
INVENTOR(S): Gibson, John W.; Miller, Stacey S.; Middleton, John C.; Tipton, Arthur J.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 699,002.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

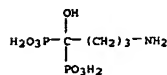
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004101557	A1	20040527	US 2002-316441	20021210
US 5747058	A	19980505	US 1995-474337	19950607
US 6415536	B1	20020702	US 1999-385107	19990827
WO 2004052336	A2	20040624	WO 2003-US39311	20031210
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 1995-474337	A2	19950607		
US 1995-478450	B2	19950607		
US 1997-944022	A2	19970915		
US 1999-385107	A3	19990827		
US 2000-699002	A2	20001026		
US 2002-316441	A	20021210		

AB The present invention relates to novel nonpolymeric compds. and compns. that form liquid, high viscosity materials suitable for the delivery of biol. active substances in a controlled fashion, and for use as medical or surgical devices. The materials can optionally be diluted with a solvent to form a material of lower viscosity, rendering the material easy to administer. This solvent may be water insol. or water soluble, where the water soluble solvent rapidly diffuses or migrates away from the material in vivo, leaving a higher viscosity liquid material. 1,6-Hexanediol lactate  $\epsilon$ -hydroxycaproic acid produced in was dissolved in N-methylpyrrolidone at a weight ratio of 70:30. Bupivacaine base (10%) was then added to this mixture. Drops weighing approx. 100 mg were precipitated into 40 mL buffer. At 4 h, around 4.1 weight of the bupivacaine contained in the precipitated drop had been released. At 24 h, around 8.6 weight

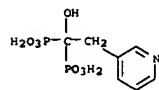
L24 ANSWER 6 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
 of the bupivacaine had been released.  
 IT 40391-99-9 66376-36-1, Alendronate 105462-24-6  
 , Risedronic acid  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (high viscosity liquid controlled drug delivery system and medical or  
 surgical device)  
 RN 40391-99-9 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX  
 NAME)



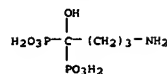
RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
 CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA  
 INDEX NAME)

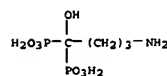


L24 ANSWER 7 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



• Na

IT 66376-36-1  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (controlled release dosage forms with core tablet  
 sheathed in annular body of compressed powder or granular material)  
 RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 7 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:219836 HCAPLUS  
 DOCUMENT NUMBER: 140:259061  
 TITLE: Controlled release dosage forms  
 with core tablet sheathed in an annular body of  
 compressed powder or granular material  
 Lerner, E. Itzhak; Rosenberger, Vered; Aqua, Ofer;  
 Flashner-Barak, Moshe  
 Israel  
 U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S.  
 Ser. No. 291,619, abandoned.  
 CODEN: USXXCO  
 Patent  
 English  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004052843	A1	20040318	US 2003-379338	20030303
BR 2003015413	A	20041214	BR 2002-15413	20021112
US 2003206954	A1	20031106	US 2003-419536	20030421
PRIORITY APPLN. INFO.:			US 2001-342442P	P 20011224
			US 2002-361821P	P 20020304
			US 2002-291619	B2 20021112
			WO 2002-US63081	W 20021112

AB The present invention provides controlled release  
 pharmaceutical dosage forms for oral administration in which a  
 core tablet is sheathed in an annular body of compressed powder or  
 granular material. A preferred embodiment of the zero-order release  
 pharmaceutical dosage form is a solid pharmaceutical  
 dosage form which reduces contact of the active ingredient in solid form  
 with the mucosa lining the gastrointestinal tract, which is particularly  
 advantageous for delivering an ulcerative drug. The drug layer may be  
 recessed from the opening of the annular body on one or both sides, and  
 the drug layer is recessed from the surface so that any contact, whether  
 with hands or with the mucosa, is with the walls of the annular body.

The annular body is preferably made of non ulcerative and non sensitive  
 pharmaceutical ingredients such as hydroxypropyl cellulose,  
 hydroxypropyl methylcellulose, microcryst. cellulose, starch, lactose,  
 sugars, polyvinyl pyrrolidone, calcium phosphate and any other regular  
 tablet excipients. A process for making the zero-order release  
 pharmaceutical dosage form are also provided.

IT 129318-43-0, Monosodium alendronate  
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (controlled release dosage forms with core tablet  
 sheathed in annular body of compressed powder or granular material)  
 RN 129318-43-0 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI)  
 (CA INDEX NAME)

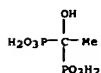
L24 ANSWER 8 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:756044 HCAPLUS  
 DOCUMENT NUMBER: 141:266048  
 TITLE: Medical implants with carbon-containing surfaces that  
 are functionalized  
 Blue Membranes GmbH, Germany  
 Ger. Gebrauchsmusterschrift, 18 pp.  
 CODEN: GGXXFR  
 Patent  
 German  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 202004009061	U1	20040916	DE 2004-202004009061	20040528
DE 10324415	A1	20041216	DE 2003-10324415	20030528
DE 10333098	A1	20050210	DE 2003-10333098	20030721
DE 10333099	A1	20050210	DE 2003-10333099	20030721
PRIORITY APPLN. INFO.:			DE 2003-10324415	A1 20030528
			DE 2003-10333098	A1 20030721
			DE 2003-10333099	A1 20030721

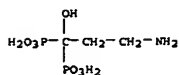
AB The invention concerns medical implants with carbon-containing surfaces  
 that are functionalized; the surfaces are prepared by (a) preparing a medical  
 implant with a carbon-containing surface; (b) activation of the carbon  
 layer by creating porosity; (c) functionalization of the activated,  
 carbon-containing layer. The carbon layer can be prepared by pyrolysis.

CVD, PVD, sputtering, ion implantation. The medical devices are prepared from  
 carbon, carbon-composite material, glass, ceramics, glass  
 fibers, carbon fibers, metals, stainless steel, titanium, tantalum,  
 platinum, nitinol, alloys, artificial bone, minerals, and their  
 combinations. Artificial blood vessels, stents, coronary stents,  
 peripheral stents, orthopedic implants, artificial hearts and heart  
 valves, artificial bones and joints are prepared. The carbon layer is  
 activated with oxidation or reducing agents in the presence of air,  
 oxygen,  
 nitrogen monoxide, oxidative acids; heat and/or ultrasound can be  
 applied.  
 The activated implant surfaces are functionalized with drugs,  
 microorganisms, plant, animal or human cells. The invention also  
 concerns

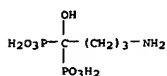
controlled-release implanted drug delivery systems.  
 IT 2809-21-4, Etidronic acid 40391-99-9 66376-36-1  
 Alendronate acid 89987-06-4, Tiludronic acid  
 105462-24-6  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (medical implants with carbon-containing surfaces that are  
 functionalized)  
 RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



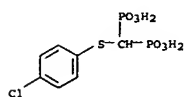
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



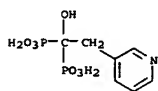
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [[[4-chlorophenyl]thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 9 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2004335684 EMBASE  
TITLE: Pharmacological management of metastatic bone pain.  
AUTHOR: Viney R.P.C.; Hayne D.; Ayra M.; Patel H.R.H.  
CORPORATE SOURCE: Dr. H.R.H. Patel, Department of Urology, Guy's Hospital, St Thomas Street, London SE1 9R, United Kingdom.  
hrhpatel@doctors.org.uk  
SOURCE: Expert Opinion on Pharmacotherapy, (2004) 5/7 (1555-1563).  
Refs: 39  
ISSN: 1465-6566 CODEN: EOPHP7  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 008 Neurology and Neurosurgery  
016 Cancer  
033 Orthopedic Surgery  
036 Health Policy, Economics and Management  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English  
AB Many malignancies metastasise to the skeleton. This often results in a relatively unique pain process, which dramatically affects a patient's quality of life. With one in three members of the population likely to develop cancer at some stage in their lives, the prevalence of bone metastases is high. Despite the large financial investment on therapies for these patients, treatment is still suboptimal [1]. In this article, the various treatments available are reviewed. Opiates and bisphosphonates, the mainstays in current practise, are covered in detail, and evolving therapies that may shape future management are also discussed. 2004 .COPYRG. Ashley Publication Ltd.

L24 ANSWER 10 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2004393283 EMBASE  
TITLE: [Supportive therapy of multiple myeloma].  
SUPPORTIVE THERAPIE DES MULTIPLIEN MYELOMS.  
AUTHOR: Zojer N.; Strasser-Weippl K.; Ludwig H.  
CORPORATE SOURCE: Dr. H. Ludwig, Medizinische Abteilung mit Onkologie, Wilhelminenspital, Montleartstrasse 37, 1160 Wien, Austria.  
Heinz.ludwig@wienkav.at  
SOURCE: Onkologe, (2004) 10/8 (843-851).  
Refs: 28  
ISSN: 0947-8965 CODEN: ONKOP4  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 006 Internal Medicine  
016 Cancer  
025 Hematology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: German

SUMMARY LANGUAGE: English; German  
AB During the last decade, the life expectancy of patients with multiple myeloma has improved significantly, mainly due to more efficient anti-myeloma therapy. In order to preserve a high quality of life throughout the course of the disease, comprehensive supportive therapy is necessary. The most common complications occurring in patients with myeloma are osteolytic bone lesions leading to pain and fractures, hypercalcemia, anemia with fatigue, and infections. For prevention and/or therapy of these complications a variety of measures may be required/including the administration of bisphosphonates, radiation and timely operative stabilization of osteolytic lesions to prevent pathologic fractures, adequate therapy of anemia, tailored pain therapy, rapid treatment, and prophylaxis against possible infections. Treatment success increases the patients' well-being, which is mirrored in improved quality of life.

L24 ANSWER 11 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 2004487237 EMBASE  
TITLE: Symptom management in the older adult.  
AUTHOR: Brown J.A.; Von Roenn J.H.  
CORPORATE SOURCE: j.vonroenn@northwestern.edu  
SOURCE: Clinics in Geriatric Medicine, (2004) 20/4 (621-640).  
Refs: 98  
ISSN: 0749-0690 CODEN: CGMEE6  
PUBLISHER IDENT.: S 0749-0690(04)00063-1  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 020 Gerontology and Geriatrics  
036 Health Policy, Economics and Management  
037 Drug Literature Index  
038 Adverse Reactions Titles  
039 Pharmacy

LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Palliative care begins at the time of diagnosis of a life-threatening illness and continues beyond the time of death. Defined in the broadest sense, the goal of palliative care is to provide aggressive symptom management and address the psychological and spiritual needs of the patient and the family. This article reviews the management of some symptoms commonly observed in older patients, highlighting treatment considerations specific to the older population. Ultimately the approach to symptoms must be individualized, and treatment decisions must reflect the patient's goals of care. Although symptom management in older patients may be challenging, it is possible to provide care that significantly enhances quality of life throughout the course of illness.

L24 ANSWER 12 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 2004450001 EMBASE  
TITLE: Preparation and evaluation of floating risedronate sodium Gelucire® 39/01 matrices.  
AUTHOR: Chauhan B.; Shimpi S.; Mahadik K.R.; Paradkar A.  
CORPORATE SOURCE: A. Paradkar, Department of Pharmaceutics, Bharati Vidyapeeth Deemed University, Poona College of Pharmacy, Erandwane, Pune-411038, Maharashtra, India.  
SOURCE: anant\_paradkar@yahoo.com  
Acta Pharmaceutica, (2004) 54/3 (205-214).  
Refs: 24  
ISSN: 1330-0075 CODEN: ACPHEE  
COUNTRY: Croatia  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 023 Nuclear Medicine  
037 Drug Literature Index  
039 Pharmacy

LANGUAGE: English  
SUMMARY LANGUAGE: English; Serbian

AB Incorporation of bisphosphonates in the lipid reduces gastric irritation. Only gastric retention with sustained release allows the drug to reach the duodenum and jejunum and improves the availability of bisphosphonates. Risedronate sodium and Gelucire® 39/01 floating matrices were prepared using melt solidification. The sustained release floating matrices were evaluated for in vitro and in vivo floating ability and in vitro drug release. Ageing of the matrices was studied by differential scanning calorimetry, hot stage polarizing microscopy, scanning electron microscopy and in vitro drug release. Ageing causes changes in the crystal structure of Gelucire®, which is responsible for an increase in drug release.

L24 ANSWER 13 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 2004229328 EMBASE  
TITLE: Pharmacokinetic and pharmacodynamic aspects of gastroretentive dosage forms.  
AUTHOR: Hoffman A.; Stepanyk D.; Levy E.; Eyal S.; Klausner E.; Friedman M.  
CORPORATE SOURCE: A. Hoffman, Department of Pharmaceutics, School of Pharmacy, Hebrew University of Jerusalem, P.O. Box 12065, Jerusalem 91120, Israel. ahoffman@cc.huji.ac.il  
SOURCE: International Journal of Pharmaceutics, (11 Jun 2004) 277/1-2 (141-153).  
Refs: 28  
ISSN: 0378-5173 CODEN: IJPHDE  
PUBLISHER IDENT.: S 0378-5173(04)00122-X  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
039 Pharmacy

LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Controlled release gastroretentive dosage forms (CR-GRDF) enable prolonged and continuous input of the drug to the upper parts of the gastrointestinal (GI) tract and improve the bioavailability of medications that are characterized by a narrow absorption window. CR-GRDF provide a means to utilize all the pharmacokinetic (PK) and pharmacodynamic (PD) advantages of controlled release dosage forms for such drugs. Thus, CR-GRDF may improve therapy with clinically used medications, as well as enable oral administration of drugs, or drug candidates, that hitherto had to be infused parenterally. This manuscript discusses the complexity of the PK and PD factors that influence the treatment benefits of CR-GRDF and summarizes the results of our recent in vivo investigations in animal models (rats and dogs) and in human subjects. We found that a CR-GRDF formulation was superior to the other modes of administration for levodopa and riboflavin, but not for metformin. The PK and PD rationales of GRDFs for the studied drugs are presented and discussed. We conclude that due to the complexity of the PK and PD factors for a certain drug, the rationale for continuous administration obtained by CR-GRDF should be assessed and established in vivo. .COPYRG. 2004 Elsevier B.V. All rights reserved.

L24 ANSWER 14 OF 79 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004297256 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15198426  
TITLE: Microencapsulation of hydrophilic drug substances using biodegradable polyesters. Part II: Implants allowing controlled drug release--a feasibility study using bisphosphonates.  
AUTHOR: Weidenauer U.; Bodmer D.; Kissel T.  
CORPORATE SOURCE: Department of Pharmaceutics and Biopharmacy, Philipps-University, D-35032 Marburg, Germany.  
SOURCE: Journal of microencapsulation, (2004 Mar) 21 (2) 137-49.  
Journal code: 8500513. ISSN: 0265-2048.  
PUB. COUNTRY: England; United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200409  
ENTRY DATE: Entered STN: 20040617  
Last Updated on STN: 20040915  
Entered Medline: 20040914

AB The prolonged delivery of hydrophilic drug salts from hydrophobic polymer carriers at high drug loading is an ambitious goal. Pamidronate disodium salt (APD) containing implants prepared from spray-dried microparticles were investigated using a laboratory ram extruder. An APD-containing polymer matrix consisting of an APD-chitosan implant embedded in the biodegradable polymer D,L-poly(lactide-co-glycolide acid-glucose) (PLG-GLU) was compared with a matrix system with the micronized drug distributed in the PLG-GLU. The APD-chitosan matrix system showed a triphasic release behaviour at loading levels of 6.86 and 15.54% (w/w) over 36 days under in-vitro conditions. At higher loading (31.92%), a drug burst was observed within 6 days due to the formation of pores and channels in the polymeric matrix. In contrast, implants containing the micronized drug showed a more continuous release profile over 48 days up to a loading of 31.78% (w/w). At a drug loading of 46.17% (w/w), a drug burst was observed. Using micronized drug salts and reducing the surface area available for diffusion, parenteral delivery systems for highly water-soluble drug candidates were shown to be technically feasible at high drug loadings.

L24 ANSWER 15 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
ACCESSION NUMBER: 2005027526 EMBASE  
TITLE: [News from drug research and development].  
NEUES AUS ARZNEIMITTEL-FORSCHUNG UND -ENTWICKLUNG.  
Deutsche Apotheker Zeitung, (23 Dec 2004) 144/52 (21-33).  
ISSN: 0011-9857 CODEN: DAZEA2  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: German

L24 ANSWER 16 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
ACCESSION NUMBER: 2004161336 EMBASE  
TITLE: Chitosan microspheres as a potential carrier for drugs.  
AUTHOR: Sinha V.R.; Singla A.K.; Wadhawan S.; Kaushik R.; Kumria R.; Bansal K.; Dhawan S.  
CORPORATE SOURCE: V.R. Sinha, Univ. Inst. of Pharmaceutical Sci., Panjab University, Chandigarh 160014, India. vr\_sinha@yahoo.com  
SOURCE: International Journal of Pharmaceutics, (15 Apr 2004) 274/1-2 (1-33).  
Refs: 205  
ISSN: 0378-5173 CODEN: IJPHDE  
PUBLISHER IDENT.: S 0378-5173(04)00022-5  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English  
SUMMARY LANGUAGE: English

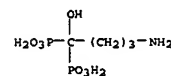
AB Chitosan is a biodegradable natural polymer with great potential for pharmaceutical applications due to its biocompatibility, high charge density, non-toxicity and mucoadhesion. It has been shown that it not only improves the dissolution of poorly soluble drugs but also exerts a significant effect on fat metabolism in the body. Gel formation can be obtained by interactions of chitosans with low molecular counterions such as polyphosphates, sulphates and crosslinking with glutaraldehyde. This gelling property of chitosan allows a wide range of applications such as coating of pharmaceuticals and food products, gel entrapment of biochemicals, plant embryo, whole cells, microorganism and algae. This review is an insight into the exploitation of the various properties of chitosan to microencapsulate drugs. Various techniques used for preparing chitosan microspheres and evaluation of these microspheres have also been reviewed. This review also includes the factors that affect the entrapment efficiency and release kinetics of drugs from chitosan microspheres.  
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L24 ANSWER 17 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN  
ACCESSION NUMBER: 2003:737555 HCAPLUS  
DOCUMENT NUMBER: 139:250322  
TITLE: Controlled release dosage forms  
INVENTOR(S): Lerner, E. Itzhak; Rosenberger, Vered; Aque, Ofer; Flashner-Barak, Moshe  
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, inc  
SOURCE: PCT Int. Appl., 59 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

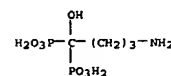
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075893	A1	20030918	WO 2003-US6591	20030303
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
BR 2002015413	A	20041214	BR 2002-15413	20021112
CA 2477701	AA	20030918	CA 2003-2477701	20030303
BR 2003008305	A	20041228	BR 2003-8305	20030303
EP 1492508	A1	20050105	EP 2003-713882	20030303
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-361821P	P 20020304
			US 2002-291619	A 20021112
			US 2001-342442P	P 20011224
			WO 2002-US63081	W 20021112
			WO 2003-US6591	W 20030303

AB A zero-order release pharmaceutical dosage form for oral administration to a patient comprises a core tablet sheathed in an annular body of compressed powder or granular material. A preferred embodiment of the zero-order release pharmaceutical dosage form is a solid pharmaceutical dosage form which reduces contact of the active ingredient in solid form with the mucosa lining the gastrointestinal tract, which is particularly advantageous for delivering an ulcerative drug. A process for making the zero-order release pharmaceutical dosage form are also provided. Oxybutynin (50 g), was mixed with anhydrous lactose (50 g) in a one pot granulator. The granulation solution, 5% KlucelTM LP (21 mL), was added with stirring until thorough mixing was achieved. The granulate was dried in the one pot granulator at 45-50° with for 20 min. The granulate was milled in a Quadro

L24 ANSWER 17 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)  
ComilTM milling machine using a screen size of 1143 µm. The oxybutynin granulate (27.6 g) was mixed with MethocelTM K15M (19 g), and compressible sucrose (Nu-TabTM, 52.4 g). Magnesium stearate (1 g) was added with mixing. The blend was compressed into tablets on a single punch tablet machine using 6 mm flat beveled punches to produce tablets weighing about 110 mg and having a hardness of 4 Kp. PEG-4000 was milled and passed through a 500-µm screen. The milled PEG-4000 (24 g), was mixed with Povidone K-30 (5 g), and Ethocel (71 g), for 3 min. Magnesium stearate (1 g), was added and the blend mixed for another 0.5 min. The inner cores, produced above, were pressed within the outer mantle by using this blend and a 9-mm outer cylinder spring loaded core rod tooling. The final product, an annular ring coated tablet with recessed exposed axial faces, had an outer diam. of 9 mm, a total wt. of 350 mg and contained 15 mg oxybutynin.  
IT 66376-36-1 Alendronate 129318-43-0, Monosodium Alendronate 600116-20-9  
RL: PKT (Pharmacokinetic); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(controlled release dosage forms)  
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

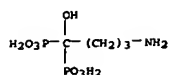


RN 129318-43-0 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 600116-20-9 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, trihydrate (9CI) (CA INDEX NAME)

●3 H<sub>2</sub>O

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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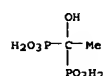
ACCESSION NUMBER: 2003:696722 HCAPLUS  
DOCUMENT NUMBER: 139:219350  
TITLE: Pharmaceutical dosage forms coated with and acrylic copolymers  
INVENTOR(S): Petereit, Hans-Ulrich; Suefke, Thomas; Meier, Christian; Schnabel, Michael; Blessing, Ingrid; Grimm, Stefan  
PATENT ASSIGNEE(S): Roehm G.m.b.H. & Co. K.-G., Germany  
SOURCE: PCT Int. Appl., 49 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072087	A1	20030904	WO 2003-EP934	20030130
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10208335	A1	20030904	DE 2002-10208335	20020227
CA 2476972	AA	20030904	CA 2003-2476972	20030130
EP 1478352	A1	20041124	EP 2003-711870	20030130
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003080006	A	20050104	BR 2003-8006	20030130
PRIORITY APPLN. INFO.:			DE 2002-10208335	A 20020227
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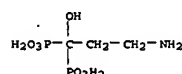
AB The invention relates to a method for producing a pharmaceutical dosage form as tablets, pellets and/or in the form of an active ingredient-containing matrix, whereby the tablets, pellets and/or active ingredient-containing matrix contain a pharmaceutical active ingredient and a copolymer serving as a coating agent and/or binding agent, and optionally contain a core and pharmaceutically common additives. According to the invention, the copolymer, the pharmaceutical active ingredient, the optionally present core and/or the pharmaceutically common additives are processed using known techniques by melting, injection molding, extrusion, wet granulation, casting, dipping, spreading out, spraying on, or pressing to form tablets, pellets and/or an active ingredient-containing matrix. The inventive method is characterized in that a copolymer is used that consists of 20 to 34 weight % methacrylic acid, 20 to 69 weight % methylacrylate and 0 to 40 weight % ethylacrylate and, optionally, of 0 to 10 weight % of addnl. vinylically copolymerizable monomers with the provision that the glass transition temperature of the copolymer is no higher than 60° according to ISO 11357-2, item 3.3.3. The invention also relates to the pharmaceutical dosage form produced according to this method, said

L24 ANSWER 18 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
copolymer and the use thereof. Thus a copolymer was prep'd. using the monomers: Me acrylate 40; Et acrylate 30; methacrylic acid 30. An emulsion polymerize contg. 30% of the copolymer was mixed with 0.85% sodium lauryl sulfate (in relation to the copolymer); the fluid was dried to a film; the film was sol. in an artificial intestinal juice at pH 6.8.  
IT 2809-21-4 40391-99-9 66376-36-1, Alendronate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical dosage forms coated with and acrylic copolymers)

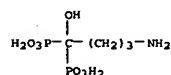
RN 2809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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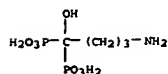
ACCESSION NUMBER: 2003:511118 HCAPLUS  
DOCUMENT NUMBER: 139:90451  
TITLE: Zero-order sustained-release dosage forms  
INVENTOR(S): Heimlich, John M.; Noack, Robert M.; Cox, Steve R.; Ganorkar, Loksidh D.; Verhage, Ronald R.; John, Lee  
E.  
PATENT ASSIGNEE(S): Pharmacia Corporation, USA  
SOURCE: PCT Int. Appl., 34 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053402	A1	20030703	WO 2002-US41104	20021219
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003133982	A1	20030717	US 2002-324719	20021219
EP 1455751	A1	20040915	EP 2002-792508	20021219
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002015262	A	20041228	BR 2002-15262	20021219
PRIORITY APPLN. INFO.:			US 2001-342642P	P 20011220
			US 2001-342819P	P 20011220
			WO 2002-US41104	W 20021219

AB The present invention relates to zero-order sustained-release solid dosage forms suitable for administration of a wide range of drugs, especially those that are water-soluble. The solid dosage form comprises (a) a matrix core comprising Et cellulose and the active agent and (b) a hydrophobic polymer coating encasing the entire matrix core. Thus, tablets contained clindamycin-HCl 76.44, Et cellulose 18.08, and Mg stearate 0.25%. Extra-granular formulations comprised Ethocel 4.99, and Mg stearate 0.25%. The coating composition comprised HPMC 10.8, and Surelease 43.2%.

IT 66376-36-1, Alendronate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (zero-order sustained-release dosage forms)  
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 19 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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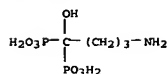
L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:491052 HCAPLUS  
DOCUMENT NUMBER: 139:57948  
TITLE: Liquid bisphosphonate formulations for bone disorders  
INVENTOR(S): Daifotis, Anastasia G.; Leung, Albert T.; Bergquist, Paul A.; Benker, Andrew  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA  
SOURCE: PCT Int. Appl., 59 pp.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051373	A1	20030626	WO 2002-US38200	20021126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZH, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003139378	A1	20030724	US 2002-305868	20021126
EP 1458400	A1	20040922	EP 2002-784653	20021126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:				US 2001-340965P P 20011213
				WO 2002-US38200 W 20021126

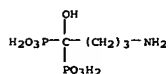
AB The present invention relates to high dose oral liquid formulations of bisphosphonate and their methods of use to treat/prevent diseases to bone remodeling or bone disorders, such as for example, Paget's disease, osteoporosis, metastatic bone disease, hypercalcemia of malignancy, periprosthetic osteolysis, periodontal disease, arthritic conditions, and the like, while minimizing the potential for esophageal irritation and other adverse gastrointestinal effects. These methods comprise orally administering to a mammal the liquid pharmaceutical composition of at least 1 bisphosphonate, or a salt, as a unit dosage according to a continuous schedule having a once-weekly, twice-weekly, biweekly, twice-monthly, or monthly dosing interval. Thus, a formulation contained alendronate monosodium trihydrate 2.454, and sodium citrate dihydrate 21.18 mg/mL, NaOH and HCl qs to pH 6.8, and water qs to 1.00 mL.

IT 66376-36-1, Alendronate 121268-17-5, Alendronate monosodium trihydrate 160055-05-8, Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



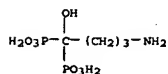
RN 121268-17-5 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



● Na

● 3 H<sub>2</sub>O

RN 260055-05-8 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)

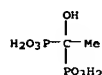


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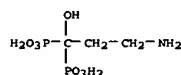
● H<sub>2</sub>O

IT 2609-21-4 40391-99-9 89987-06-4, Tiludronate  
105462-24-6 129318-43-0, MonoSodium Alendronate  
157432-53-6 160982-64-9, Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt 548457-54-1  
548457-56-3 548457-59-6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
[liquid bisphosphonate formulations for bone disorders]  
RN 2609-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

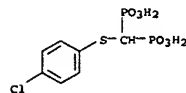
L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



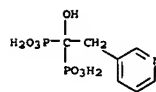
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [(4-chlorophenyl)thio]methylene)bis- (9CI) (CA INDEX NAME)

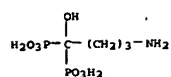


RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



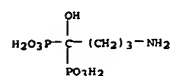
RN 129318-43-0 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



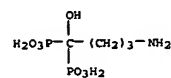
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RN 157432-53-6 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, magnesium salt (9CI)  
(CA INDEX NAME)



●x Mg

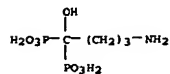
RN 160982-64-9 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt (9CI)  
(CA INDEX NAME)



●x Na

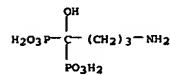
RN 548457-54-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, potassium salt (9CI)  
(CA INDEX NAME)

L24 ANSWER 20 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



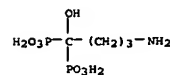
●x K

RN 548457-56-3 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (9CI)  
(CA INDEX NAME)



●x Ca

RN 548457-59-6 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, ammonium salt (9CI)  
(CA INDEX NAME)



●x NH<sub>3</sub>

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
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L24 ANSWER 21 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:334829 HCAPLUS  
DOCUMENT NUMBER: 138:343889  
TITLE: Novel pharmaceutical compounds containing  
drugs bound to polypeptides  
INVENTOR(S): Picariello, Thomas  
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA  
SOURCE: PCT Int. Appl., 4662 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 12  
PATENT INFORMATION:

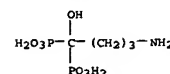
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034980	A2	20030501	WO 2001-US43089	20011114
WO 2003034980	C1	20031120		
W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RN: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2428971	AA	20030501	CA 2001-2428971	20011114
EP 1401374	A1	20040331	EP 2001-274606	20011114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.: US 2000-274622P P 20001114				
US 2000-247622P P 20001114				
WO 2001-US43089 W 20011114				

AB Comps. comprising polypeptides and drugs covalently attached to the polypeptide are disclosed. Also provided is a method for delivery of these drugs to a patient comprising administering to the patient a composition comprising a polypeptide and a drug covalently attached to the polypeptide. Also provided is a method for protecting drugs from degradation comprising covalently attaching them to a polypeptide. Also provided is a method for controlling release of drugs from a composition comprising covalently attaching them to the polypeptide.

IT 66376-36-1DP, Alendronate, protein conjugates  
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(novel pharmaceutical compds. containing drugs bound to polypeptides)

RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 21 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:202410 HCAPLUS  
DOCUMENT NUMBER: 138:226705  
TITLE: Novel pharmaceuticals comprising drug  
conjugates with polypeptide carriers  
INVENTOR(S): Picariello, Thomas  
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA  
SOURCE: PCT Int. Appl., 2059 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 12  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020200	A2	20030313	WO 2001-US43117	20011116
WO 2003020200	A3	20030912		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2429345	AA	20030313	CA 2001-2429345	20011116
EP 1357928	A2	20031105	EP 2001-273387	20011116
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			

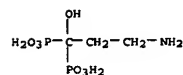
PRIORITY APPLN. INFO.: US 2000-248600P P 20001116

L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
US 2000-248695P P 20001116  
US 2000-248696P P 20001116  
US 2000-248697P P 20001116  
US 2000-248698P P 20001116  
US 2000-248701P P 20001116  
US 2000-248702P P 20001116  
US 2000-248703P P 20001116  
US 2000-248704P P 20001116  
US 2000-248705P P 20001116  
US 2000-248706P P 20001116  
US 2000-248707P P 20001116  
US 2000-248708P P 20001116  
US 2000-248709P P 20001116  
US 2000-248710P P 20001116  
US 2000-248711P P 20001116  
US 2000-248712P P 20001116  
US 2000-248686P P 20001116  
US 2000-248688P P 20001116  
US 2000-248714P P 20001116  
US 2000-248715P P 20001116  
US 2000-248716P P 20001116  
US 2000-248717P P 20001116  
US 2000-248718P P 20001116  
US 2000-248719P P 20001116  
US 2000-248720P P 20001116  
US 2000-248748P P 20001116  
US 2001-248664P P 20011116  
US 2001-248665P P 20011116  
US 2001-248666P P 20011116  
US 2001-248667P P 20011116

L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
US 2001-248668P P 20011116  
US 2001-248669P P 20011116  
US 2001-248671P P 20011116  
US 2001-248672P P 20011116  
US 2001-248673P P 20011116  
US 2001-248674P P 20011116  
US 2001-248675P P 20011116  
US 2001-248676P P 20011116  
US 2001-248677P P 20011116  
US 2001-248678P P 20011116  
US 2001-248679P P 20011116  
US 2001-248680P P 20011116  
US 2001-248681P P 20011116  
US 2001-248682P P 20011116  
US 2001-248683P P 20011116  
US 2001-248684P P 20011116  
US 2001-248765P P 20011116  
US 2001-248766P P 20011116  
US 2001-248767P P 20011116  
US 2001-248773P P 20011116  
US 2001-248774P P 20011116  
US 2001-248775P P 20011116  
US 2001-248778P P 20011116  
US 2001-248780P P 20011116  
US 2001-248781P P 20011116  
US 2001-248783P P 20011116  
US 2001-248784P P 20011116  
US 2001-248785P P 20011116  
US 2001-248786P P 20011116  
US 2001-248787P P 20011116

L24 ANSWER 22 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
US 2001-248790P P 20011116  
US 2001-248791P P 20011116  
US 2001-248792P P 20011116  
US 2001-248793P P 20011116  
US 2001-248833P P 20011116  
US 2001-248848P P 20011116  
US 2001-248849P P 20011116  
WO 2001-US43117 W 20011116

AB A pharmaceutical composition comprising a polypeptide and an active agent attached to said polypeptide is disclosed.  
IT 40391-99-9D, polypeptide conjugates  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(novel pharmaceuticals comprising drug conjugates with polypeptide carriers)  
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 23 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:154278 HCAPLUS  
 DOCUMENT NUMBER: 138:198670  
 TITLE: GnRH agonist combination drugs  
 INVENTOR(S): Furuya, Shuichi; Kuwaka, Masami  
 PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan  
 SOURCE: PCT Int. Appl., 73 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015620	A1	20030227	WO 2001-JP8130	20020808
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
TM	RM: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
JP 2003137814	A2	20030514	JP 2002-231922	20020808
EP 1424080	A1	20040602	EP 2002-758814	20020808
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			JP 2001-244616	A 20010810
			WO 2002-JP8130	W 20020808

AB In the field of pharmaceuticals, it is intended to provide drugs whereby the preventive and therapeutic effects of a GnRH agonist on various diseases can be enhanced and QOL can be improved. More specifically, combination drugs characterized in that the GnRH agonist is combined with a chemical selected from among SERM, SARM, sex hormone synthesis inhibitors, receptor-type tyrosine kinase inhibitors, bone metabolism regulators, drugs for immunotherapy, cytokine/chemokine inhibitors and endothelin receptor antagonists. Owing to these combinations, excellent effects of enhancing the preventive and therapeutic effects of the GnRH agonist on various diseases and relieving side effects can be established. Furthermore, QOL can be improved thereby.

IT 2809-21-4, Etidronic acid 40391-99-9, Pamidronic acid 66376-36-1, Alendronic acid 105462-24-6, Risedronic acid  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (GnRH agonist combination drugs for treating various diseases and relieving side effects)

RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

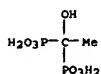
L24 ANSWER 24 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:176580 HCAPLUS  
 DOCUMENT NUMBER: 138:126974  
 TITLE: Dosage forms for immediate gastric release of a calcium transport stimulator coupled with delayed gastric release of a bis-phosphonate  
 INVENTOR(S): Fleishner-Barak, Moshé  
 PATENT ASSIGNEE(S): Teva Pharmaceuticals USA, Inc.  
 SOURCE: PCT Int. Appl., 24 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007916	A1	20030110	WO 2002-US22825	20020717
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1416919	A1	20040512	EP 2002-750134	20020717
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-305913P	P 20010717
			WO 2002-US22825	W 20020717

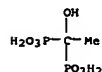
AB The present invention provides a gastric retention dosage form for immediate or uncontrolled release of a vitamin D derivative that stimulates calcium absorption from the intestine, like calcitriol, alphacalcidol and calcifediol, combined with delayed release of a bis-phosphonate calcium resorption inhibitor such as alendronic acid and its pharmaceutically acceptable salts and hydrates.

IT 2809-21-4 66376-36-1, Alendronic acid 89987-06-4  
 2, Tiludronate 105462-24-6 121268-17-5  
 260055-05-8  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dosage forms for immediate gastric release of calcium transport stimulator coupled with delayed gastric release of bis-phosphonate)

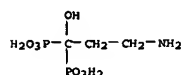
RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



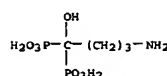
L24 ANSWER 23 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



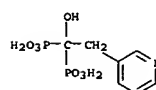
RN 40391-99-9 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
 CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

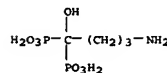


REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

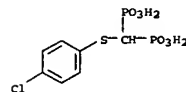
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L24 ANSWER 24 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

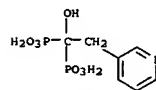
RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



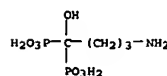
RN 89987-06-4 HCAPLUS  
 CN Phosphonic acid, [(4-chlorophenyl)thio]methylene)bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
 CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



RN 121268-17-5 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)

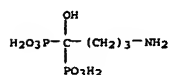


● Na

● 3 H<sub>2</sub>O

L24 ANSWER 24 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 260055-05-8 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)



● Na

● H<sub>2</sub>O

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L24 ANSWER 25 OF 79 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:64836 BIOSIS  
DOCUMENT NUMBER: PREV200400065894  
TITLE: Preparation of 1-hydroxyethylidene-1,1-diphosphonic acid-intercalated layered double hydroxide and its physicochemical properties.  
AUTHOR(S): Nakayama, Hirokazu [Reprint Author]; Takeshita, Koji; Tsuchioka, Mitsutomo  
CORPORATE SOURCE: Department of Functional Molecular Chemistry, Kobe Pharmaceutical University, 4-19-1 Motoyamakitamachi, Higashinada-ku, Kobe, 658-8558, Japan  
SOURCE: Journal of Pharmaceutical Sciences, (December 2003) Vol. 92, No. 12, pp. 2419-2426, print.  
CODEN: JPMSAE. ISSN: 0022-3549.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 28 Jan 2004  
Last Updated on STN: 28 Jan 2004

AB The intercalation of 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP), which is a drug for osteoporosis, in layered double hydroxide (LDH) was examined with the goal of developing a novel drug delivery system (DDS) of HEDP. To prevent side reactions, the intercalation reaction was carried out at 0 degreeC, and at pH 4-6. The uptake of HEDP was determined as 3.5 mmol g-1 of LDH, and the interlayer distance increased from 7.8 to 13 ANG. The HEDP-release profiles into K2CO3 aqueous solution and into various buffer solutions were also examined.

L24 ANSWER 26 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003432402 EMBASE  
TITLE: Drug-Induced Esophageal Injuries and Dysphagia.  
AUTHOR: O'Neill J.L.; Remington T.L.  
CORPORATE SOURCE: T.L. Remington, University of Michigan Health System, Department of Pharmacy UM B2 D301, 1500 E. Medical Center Dr., Ann Arbor, MI 48109-0008, United States.  
SOURCE: Annals of Pharmacotherapy, (2003) 37/11 (1675-1684).  
Refs: 110  
ISSN: 1060-0280 CODEN: APHRER  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 037 Drug Literature Index  
038 Adverse Reactions Titles  
039 Pharmacy  
048 Gastroenterology  
LANGUAGE: English  
SUMMARY LANGUAGE: English; Spanish; French

AB OBJECTIVE: To review and analyze medical literature documenting drug-induced esophageal injury and dysphagia and to formulate strategies to enhance pharmacists' prevention, detection, and treatment of these iatrogenic complications. DATA SOURCES: A MEDLINE search (1966-April 2002) was conducted to identify primary and secondary literature using variable combinations of the following search terms: pill-induced, drug-induced, or iatrogenic with esophageal injury, esophageal damage, or dysphagia. Bibliographies were also reviewed to identify additional relevant references. STUDY SELECTION AND DATA EXTRACTION: All case reports, reviews, and clinical studies relating to drug-induced esophageal injury or swallowing dysfunction were evaluated. DATA SYNTHESIS: Drug-induced esophageal injury may be under-recognized. Several drugs have been associated with physical or chemically mediated injuries. Risk factors for injury have been identified and preventive and treatment strategies have been successful in limiting esophageal injury. Drug-induced dysphagia can have serious complications and is most often associated with typical neuroleptics such as haloperidol. CONCLUSIONS: Pharmacists can play a pivotal role in proactively identifying situations where there is a higher likelihood of drug-induced esophageal injury or dysphagia. They can recommend preventive strategies to promote safe medication use, help identify iatrogenic complications when they occur, and assist in formulation of appropriate treatment strategies.

L24 ANSWER 27 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

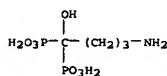
ACCESSION NUMBER: 2003:383077 HCAPLUS  
DOCUMENT NUMBER: 140:117159  
TITLE: Oral pharmaceutical formulations for bone resorption inhibitor  
AUTHOR(S): Anon.  
CORPORATE SOURCE: UK  
SOURCE: Research Disclosure (2003), 468(April), P523 (No. 467143)  
CODEN: RSDSBB; ISSN: 0374-4353  
PUBLISHER: Kenneth Mason Publications Ltd.  
DOCUMENT TYPE: Journal; Patent  
LANGUAGE: English  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RD 467143		20030310		

PRIORITY APPLN. INFO.: RD 2003-467143 20030310  
AB The chemical formula is presented of an active ingredient in oral formulations for bone resorption inhibitor. Ingredients and dosage forms of the formulation are described.

IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oral pharmaceutical formulations for bone resorption inhibitor)

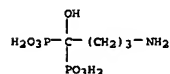
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



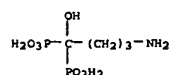
L24 ANSWER 28 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 ACCESSION NUMBER: 2004037637 EMBASE  
 TITLE: A case history illustrating how extended release cholinesterase inhibitors could improve management of Alzheimer's disease [1].  
 AUTHOR: Aliak J.M.  
 CORPORATE SOURCE: J.M. Aliak, Marshfield Clin. Research Foundation, Marshfield Clinic-Thorp Center, 1000 Oak Avenue, Marshfield, WI 54449, United States.  
 SOURCE: Aliak.Joseph@marshfieldclinic.org  
 Journal of Alzheimer's Disease, (2003) 5/6 (477-478).  
 ISSN: 1387-2877 CODEN: JADIF  
 Netherlands  
 COUNTRY: Journal; Letter  
 DOCUMENT TYPE: 008 Neurology and Neurosurgery  
 FILE SEGMENT: 020 Gerontology and Geriatrics  
 037 Drug Literature Index  
 039 Pharmacy  
 LANGUAGE: English

L24 ANSWER 29 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 ACCESSION NUMBER: 2003440086 EMBASE  
 TITLE: Polyphosphates and Other Phosphorus-Containing Polymers for Drug Delivery Applications.  
 AUTHOR: Chaubal M.V.; Gupta A.S.; Lopina S.T.; Bruley D.F.  
 CORPORATE SOURCE: M.V. Chaubal, Baxter Healthcare, Route 120 and Wilson Road, Round Lake, IL 60073, United States  
 SOURCE: Critical Reviews in Therapeutic Drug Carrier Systems, (2003) 20/4 (295-315).  
 Refs: 62  
 ISSN: 0743-4863 CODEN: CRTSED  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 037 Drug Literature Index  
 039 Pharmacy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Poly(phosphate ester)s, polyphosphonates, and polyphosphazenes are three classes of phosphorus-containing polymers that have received wide attention over the past decade for their utility in biomedicine and tissue engineering. These three families of polymers can lead to a number of subclasses of polymers with varied properties. Significant research in this area has led to niche polymers with morphologies ranging from viscous gels to amorphous microparticles for utility in drug delivery. Furthermore, the pentavalency of phosphorus offers the potential for covalent linking of the drug. The classes of polymers discussed in this review are being explored in human clinical trials for vaccine delivery as well as delivery of oncolytic and CNS therapeutics. More applications in the areas of DNA delivery and tissue engineering are also being explored.

L24 ANSWER 30 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:486649 HCAPLUS  
 DOCUMENT NUMBER: 140:258856  
 TITLE: Oral pharmaceutical formulations for bone resorption inhibitor  
 AUTHOR(S): Anon.  
 CORPORATE SOURCE: USA  
 SOURCE: IP.com Journal (2003), 3(4), 61 (No. IFCOM000011782D)  
 14 Mar 2003  
 CODEN: IJPOBX; ISSN: 1533-0001  
 PUBLISHER: IP.com, Inc.  
 DOCUMENT TYPE: Journal; Patent  
 LANGUAGE: English  
 PATENT INFORMATION:  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 IP 11782D 20030314 IP 2003-11782D 20030314  
 PRIORITY APPLN. INFO.:  
 AB Sustained, controlled or immediate release oral dosage forms capable of releasing the active pharmaceutical ingredient, optionally in the form of its monosodium salt trihydrate, to human patients immediately or over extended periods following administration are reported.  
 IT 66376-36-1 129318-43-0  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study);  
 USES  
 (Uses)  
 (oral pharmaceutical formulations for bone resorption inhibitor)  
 RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 129318-43-0 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

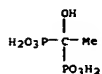


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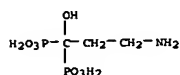
L24 ANSWER 31 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:813899 HCAPLUS  
 DOCUMENT NUMBER: 137:299972  
 TITLE: Modification of the sustained-release profile of a drug by a biocompatible polymer and a bisphosphonate  
 INVENTOR(S): Dasch, James R.; Riley, M. Gary I.  
 PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA  
 SOURCE: PCT Int. Appl., 49 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 WO 2002083096 A1 20021024 WO 2002-US8440 20020319  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, NO, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TW, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 US 2003004100 A1 20030102 US 2001-835001 20010413  
 US 6558702 B2 20030506  
 CA 2444421 AA 20021024 CA 2002-2444421 20020319  
 EP 1395240 A1 20040310 EP 2002-709857 20020319  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004532218 T2 20041021 JP 2002-580900 20020319  
 US 2003236192 A1 20031225 US 2003-400162 20030325  
 US 2004147488 A1 20040729 US 2004-758717 20040116  
 PRIORITY APPLN. INFO.:  
 WO 2002-US8440 W 20020319  
 US 2003-400162 A1 20030325

AB The present invention relates to a method for the sustained release in vivo of a biol. active agent comprising administering to a subject in need of treatment an effective amount of a sustained-release composition comprising a biocompatible polymer having the biol. active agent incorporated therein, and a bisphosphonate wherein the bisphosphonate compound is present in an amount sufficient to modify the release profile of the biol. active agent from the sustained-release composition  
 Pharmaceutical compns. suitable for use in the method of the invention are also disclosed.  
 IT 2809-21-4 57248-88-1 66376-36-1, Alendronate  
 89987-06-4, Tiludronate 115436-72-1  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (modification of sustained-release profile of drug by biocompatible polymer and bisphosphonate)  
 RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 31 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

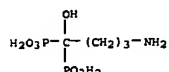


RN 57248-88-1 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

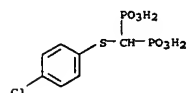


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RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

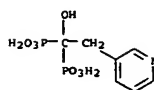


RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [[(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 115436-72-1 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 31 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L24 ANSWER 32 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:615414 HCAPLUS  
DOCUMENT NUMBER: 137:159355  
TITLE: Compositions containing bisphosphonates for management of bone density  
INVENTOR(S): Chan, Tai Wah  
PATENT ASSIGNEE(S): Direct Corporation, USA  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXKD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062352	A2	20020815	WO 2002-US3794	20020207
WO 2002062352	A3	20030403		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, T2, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2438208	AA	20020815	CA 2002-2438208	20020207
US 2002151876	A1	20021017	US 2002-71821	20020207
EP 1365770	A2	20031203	EP 2002-718929	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2001-267323P	P 20010207
			WO 2002-US3794	W 20020207

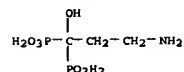
AB The invention features devices and methods for the delivery of a formulation to an individual to stabilize or increase bone mass by increasing bone deposition and/or decreasing bone resorption. In the present invention, a drug formulation comprising a bisphosphonate is provided parenterally in a sustained release dosage form, e.g., as an injected matrix or stored within a drug delivery device.

In a specific embodiment, the dosage form may be implanted or injected into a site in the body (i.e., implantation site) and a conduit, e.g., a catheter, can be used to transport the formulation from the dosage form for release at a site in the body distal from the implantation site. Pamidronate sodium was reconstituted with 10 mL phosphate buffered saline to achieve a concentration of 9 mg/mL. The 9 mg/mL solution was then diluted to achieve a concentration of 0.9 mg/mL.

IT 57248-88-1, Disodium Pamidronate  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compos. containing bisphosphonates for management of bone d.)

RN 57248-88-1 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 32 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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Searched by: Mary Hale 571-272-2507 REM 1D86

L24 ANSWER 33 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2002:555334 HCAPLUS  
DOCUMENT NUMBER: 137:114525  
TITLE: Syntactic deformable pharmaceutical foam compositions  
INVENTOR(S): Odidi, Ise; Odidi, Amina  
PATENT ASSIGNEE(S): Can.  
SOURCE: PCT Int. Appl., 47 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002056861	A2	20020725	WO 2002-CA54	20020117
WO 2002056861	A3	20021017		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6800668	B1	20041005	US 2001-765783	20010119
CA 2435276	AA	20020725	CA 2002-2435276	20020117
PRIORITY APPLN. INFO.:			US 2001-765783	A 20010119
			WO 2002-CA54	W 20020117

AB The invention relates to methods for preparing a syntactic foam compo-  
suitable for use as a carrier for chems. or other compds., including  
pharmaceuticals. Carbopol 971P, hydroxyethyl cellulose, cellulose  
microspheres and silica, was mixed in a high-shear mixer. The resulting  
admixt. was treated with 2-propanol, while simultaneously subjecting the  
admixt. to high-shear forces in the high-shear mixer. This mixing  
created  
a uniform stable syntactic deformable and compressible dendritic solid  
foam which could be shaped before drying. Metoprolol succinate was added  
to the above admixt. and subjected to high-shear agitation for 2 min  
before treatment with 2-propanol. A stable syntactic deformable and  
compressible dendritic solid foam which could be shaped before drying was  
obtained. This was dried at 40°. The dried foam was the  
disentangled by size reduction to obtain discrete particles. The free  
flowing  
particles were reassembled and shaped by compression in a mold. The  
shaped units, when subjected to an aqueous medium, released metoprolol  
over a  
period of 53 h.  
IT 66376-36-1. Alendronate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(syntactic deformable pharmaceutical foam compo.)  
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

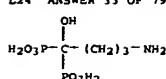
L24 ANSWER 34 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2002:107047 HCAPLUS  
DOCUMENT NUMBER: 136:156434  
TITLE: Vaginal delivery of bisphosphonates  
INVENTOR(S): Harrison, Donald C.; Liu, James H.  
PATENT ASSIGNEE(S): UMD, Inc., USA  
SOURCE: PCT Int. Appl., 68 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009631	A1	20020207	WO 2001-US22205	20010712
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6572874	B1	20030603	US 2000-626025	20000727
AU 765269	B2	20030911	AU 2001-54192	20010703
EP 1311213	A1	20030521	EP 2001-957150	20010712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013134	A	20040622	BR 2001-13134	20010712
JP 2004519420	T2	20040702	JP 2002-515186	20010712
NO 2003000422	A	20030311	NO 2003-422	20030127
PRIORITY APPLN. INFO.:			US 2000-626025	A 20000727
			US 1998-79897	A2 19980515
			AU 1998-76976	A3 19980610
			US 1999-146218P	P 19990728
			WO 2001-US22205	W 20010712

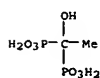
AB A targeted site delivery of bisphosphonates to the vagina using a  
medicated intravaginal device comprising a bisphosphonate composition  
formulated for transvaginal delivery is described. A method for  
treatment  
of osteoporosis and related bone and skeleton diseases, for prevention of  
bone breakdown and loss of bone mass and strength by intravaginal  
administration of bisphosphonates to the vagina and transvaginal delivery  
of bisphosphonates to the general circulation. For example, vaginal  
suppositories were prepared containing alendronate (14 mg/kg body  
weight) using  
Suppocire AS2 (75%), hydroxypropyl Me cellulose (10%), as a mucoadhesive  
agent, and Transcutol (15%), as a penetration enhancer.  
IT 2809-21-4 40391-99-9 66376-36-1, Alendronate  
89987-06-4, Tiludronate 105462-24-6  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(vaginal delivery of bisphosphonates for treatment of osteoporosis and

L24 ANSWER 33 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)

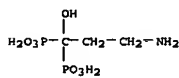


L24 ANSWER 34 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)

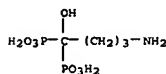
related bone diseases)  
RN 2809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



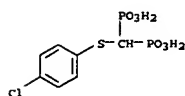
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



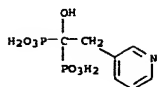
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ACCESSION NUMBER: 2002:71846 HCAPLUS  
DOCUMENT NUMBER: 136:123663  
TITLE: Pharmaceutical composition improved in peroral absorbability  
INVENTOR(S): Watanabe, Shunsuke; Takemura, Shigeo; Tautsui, Yuuki; Kondo, Hiroshi; Nakanishi, Kiyo; Sako, Kazuhiro; Sawada, Toyohiro  
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 60 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

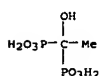
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005786	A1	20020124	WO 2001-JP6135	20010716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2415643	AA	20020124	CA 2001-2415643	20010716
US 2002150624	A1	20021017	US 2001-907557	20010716
EP 1302201	A1	20030416	EP 2001-949994	20010716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 3563070	B2	20040908	JP 2002-511719	20010716
JP 2004083601	A2	20040318	JP 2003-419042	20031217
PRIORITY APPLN. INFO.: US 2000-218980P P 20000717				
JP 2002-511719 A3 20010716				
WO 2001-JP6135 W 20010716				

AB Disclosed is a pharmaceutical composition improved in peroral absorbability, which comprises a drug, aminoalkyl methacrylate copolymer E, and an acid substance and in which the three components stand adjacent to each another and at least the copolymer and the acid substance are uniformly dispersed; a method for improving peroral absorbability by using the composition; and a peroral absorption improver for enhancing the penetration of drug into the gastrointestinal mucosa and/or the mucous blanket present on the surface thereof, which contains aminoalkyl methacrylate copolymer E as the active ingredient. A powder was prepared by mixing and drying of Bu methacrylate-dimethylaminoethyl methacrylate-Me methacrylate copolymer (Eudragit E100)/Tween 80 (10:1) 1650 and 1 M HCl/ethanol (5:12) 12000 g. The obtained powder 125 mg was combined with [1-Hydroxy-2-imidazo-(1,2-a)pyridin-3-ylethylidene]bis-phosphonate 10 and lactose 65 mg to obtain a tablet showing improved Cmax and AUC values in dog.

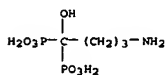
IT 2809-21-4 66376-36-1, Alendronate  
RL: PKT (Pharmacokinetics); THRU (Therapeutic use); BIOL (Biological)

study); USES (Uses)  
(pharmaceutical compo. having improved peroral absorbability contg. drugs, aminoalkylmethacrylate copolymer E, and acids)

RN 2809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ACCESSION NUMBER: 2002:10272 HCAPLUS  
DOCUMENT NUMBER: 136:74650  
TITLE: Rapidly expanding composition for gastric retention and controlled release of therapeutic agents  
INVENTOR(S): Fleshner-Barak, Moshe; Lerner, E. Itzhak; Rosenberger, Vered; Dahan, Mazal; Imakov, Yisrael  
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.  
SOURCE: PCT Int. Appl., 67 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

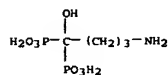
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000213	A1	20020103	WO 2001-US20134	20010622
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2412490	AA	20020103	CA 2001-2412490	20010622
EP 1305021	A1	20030502	EP 2001-946709	20010622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501190	T2	20040115	JP 2002-504995	20010622
US 2003203878	A1	20031030	US 2003-420403	20030422
PRIORITY APPLN. INFO.: US 2000-213832P P 20000623				
US 2000-217110P P 20000710				
US 2000-223212P P 20000804				
US 2001-260438P P 20010109				
US 2001-770898 A1 20010126				
WO 2001-US20134 W 20010622				
US 2002-246502 B1 20020916				

AB The present invention provides a pharmaceutical composition for use in a dosage form for oral administration to a patient. The composition expands upon contact with gastric fluid and promotes retention of the dosage form in the patient's stomach for a prolonged period of time. The present invention further provides pharmaceutical dosage forms containing an active ingredient, and the pharmaceutical composition. The forms are adapted for immediate or controlled release of the active ingredient. The dosage forms may be used advantageously in the treatment of Parkinson's disease with levodopa and hyperactivity and attention

L24 ANSWER 36 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
deficit disorder with methylphenidate. A tablet contained sodium  
alendronate monohydrate 1.67, hydroxypropyl Me cellulose 16.7,  
hydroxypropyl cellulose 56.6, croscarmellose sodium 14, tannic acid 10,  
and magnesium stearate 15. The cumulative release of alendronate from  
the  
tablet after 24 h was 45%.

IT 185959-98-2  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(rapidly expanding composition for gastric retention and  
controlled release of therapeutic agents)

RN 185959-98-2 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt,  
monohydrate (9CI) (CA INDEX NAME)



● 2 Na

● H<sub>2</sub>O

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2002:10265 HCAPLUS  
DOCUMENT NUMBER: 136:74647  
TITLE: Composition and dosage form for delayed  
gastric release of alendronate and/or other  
bis-phosphonates  
INVENTOR(S): Flashner-Barak, Moshe; Rosenberger, Vered; Dahan,  
Mazal; Lerner, Yitzhak  
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva  
Pharmaceuticals USA, Inc.  
SOURCE: PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

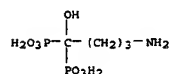
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000204	A1	20020103	WO 2001-US20130	20010622
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002015733	A1	20020207	US 2001-770898	20010126
US 6476006	B2	20021105		
CA 2412024	AA	20020103	CA 2001-2412024	20010622
EP 1296657	A1	20030402	EP 2001-946706	20010622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501186	T2	20040115	JP 2002-504986	20010622
US 2003203878	A1	20031030	US 2003-420403	20030422
PRIORITY APPLN. INFO.:			US 2000-213832P	P 20000623
			US 2001-260438P	P 20010109
			US 2001-770898	A 20010126
			WO 2001-US20130	W 20010622
			US 2002-246502	B1 20020916

AB The present invention provides compacted pharmaceutical  
compos. for oral administration to a patient which expands upon  
contact with gastric fluid to retain a dosage form in the patient's  
stomach for an extended period of time, the formulation comprising a  
non-hydrated hydrogel, a superdisintegrant and tannic acid. The present  
invention further provides a pharmaceutical dosage form containing  
an active ingredient, and the compacted pharmaceutical  
composition. The invention further provides a dosage form suitable for  
delivering a therapeutic bisphosphonate such as alendronate to the  
stomach  
of a patient over an extended period. Thus, an extended-release tablet  
formulation contained HPMC 15.9, hydroxypropyl cellulose 47.6, sodium  
starch glycolate 31.7, and tannic acid 4.8%. Sodium alendronate

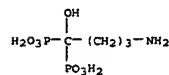
L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
formulated in another tablet formulation was incorporated into the above  
tablet formulation. The tablets obtained had good mech. strength.

IT 66376-36-1, Alendronic acid 66376-36-1D, Alendronic  
acid, salts 121268-17-5 260055-05-8  
385396-33-8  
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological  
study); USES (Uses)  
(dosage forms for delayed gastric release of alendronate and/or other  
bisphosphonates)

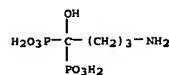
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 121268-17-5 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt,  
trihydrate (9CI) (CA INDEX NAME)

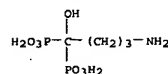


● Na

● 3 H<sub>2</sub>O

RN 260055-05-8 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt,  
monohydrate (9CI) (CA INDEX NAME)

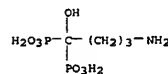
L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

● H<sub>2</sub>O

RN 385396-33-8 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt,  
monohydrate (9CI) (CA INDEX NAME)

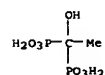


● x Na

● H<sub>2</sub>O

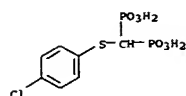
IT 3809-21-4 89987-06-4, Tiludronate 105462-34-6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(dosage forms for delayed gastric release of alendronate and/or other  
bisphosphonates)

RN 3809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

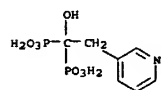


RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [((4-chlorophenyl)thio)methylene]bis- (9CI) (CA INDEX  
NAME)

L24 ANSWER 37 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



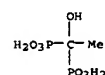
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L24 ANSWER 38 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:951507 HCAPLUS  
DOCUMENT NUMBER: 142:246092  
TITLE: Implantable sustained release formulation of bisphosphonate bone resorption inhibitor  
INVENTOR(S): Kang, Gil Seon; Kim, Hyeon Jong; Kim, Sang Uk; Lee, Hae Bang; Lee, Jeong Sik; Sung, Ha Su  
PATENT ASSIGNEE(S): Korea Research Institute of Chemical Technology, S. Korea  
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given  
CODEN: KRXXXA7  
DOCUMENT TYPE: Patent  
LANGUAGE: Korean  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

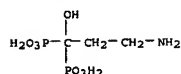
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2002080018	A	20021023	KR 2001-19043	20010410
PRIORITY APPLN. INFO.:			KR 2001-19043	20010410

AB A sustained release formulation obtained by inclusion of bisphosphonate as an inhibitor of bone resorption into a biodegradable polymer and formulation thereof into an implant type is provided which can be administered to the effected part of a patient suffering from bone disease by injection or operation, etc. This sustained release formulation comprises 0.01 to 70% by weight of a bisphosphonate based bone resorption inhibitor and 30 to 99.99% by weight of a biodegradable polymer and is in the shape of 0.1 μ to 20mm fine particles, microsphere, microcapsule, fine powder and paste. The bisphosphonate based bone resorption is one or more selected from Etidronate, Clodronate, Tiludronate, Pamidronate, Alendronate, Risedronate, Ibandronate, Zoledronate and a pharmaceutically acceptable salt, hydrate and a partial hydrate thereof.  
IT 2809-21-4 40391-99-9 66376-36-1, Alendronate  
89987-06-4, Tiludronate 105462-24-6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (implantable sustained release formulation of bisphosphonate bone resorption inhibitor)  
RN 2809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

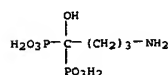


RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

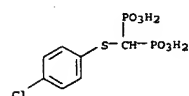
L24 ANSWER 38 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



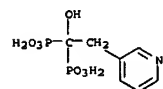
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)



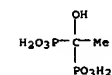
L24 ANSWER 39 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:693116 HCAPLUS  
DOCUMENT NUMBER: 137:222060  
TITLE: Method for manufacture of pharmaceutical granules  
INVENTOR(S): Ochiai, Yasushi; Wakiesaka, Kouji  
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan  
SOURCE: Eur. Pat. Appl., 43 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

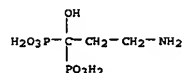
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238662	A2	20020911	EP 2002-5224	20020307
EP 1238662	A3	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002332226	A2	20021122	JP 2002-61478	20020307
US 2003039699	A1	20030227	US 2002-91559	20020307
PRIORITY APPLN. INFO.:			JP 2001-64056	A 20010307

AB Coated pharmaceutical granules contain a water-soluble drug as an active ingredient at a high d., which is superior in uniform content and stability, and which is capable of providing a pharmaceutical formulation superior in drug release control and having a smaller size than conventional preps., and a production method for the manufacture of granules. By using a rotary fluidized-bed granulation apparatus, an aqueous solution of metformin-HCl was sprayed on single crystals of the drug charged in the apparatus. The granules were dried, and after drying, the granules were sieved to give granules with a particle size of 500-840 μm.  
IT 7414-83-7, Sodium ethidronate  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (method for manufacture of pharmaceutical granules)

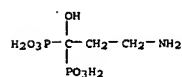
RN 7414-83-7 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2002:782875 HCAPLUS  
 DOCUMENT NUMBER: 138:326449  
 TITLE: Preparation and characterization of pamidronate-loaded PLGA wafer for the treatment of bone resorption  
 AUTHOR(S): Yoo, Je-Young; Kim, Sang Wook; Khang, Gilson; Seong, Ha Soo; Jeong, Je Kyo; Kim, Hyung Jong; Lee, Jung Sik;  
 CORPORATE SOURCE: Lee, Hai Bang  
 Dept. of Advanced Organic Materials Eng., Chonbuk National Univ., Jeonju, 561-756, S. Korea  
 SOURCE: Polymer (Korea) (2002), 26(5), 680-690  
 CODEN: POLLDG; ISSN: 0379-153X  
 PUBLISHER: Polymer Society of Korea  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Korean  
 AB Implantable biodegradable wafers were prepared with pamidronate-loaded poly(L-lactide-co-glycolide) (PLGA, 75:25 mol ratio by lactide to glycolide, mol. weight; 20000 and 90000 g/mol) by direct compression method for the sustained release of pamidronate to investigate the possibility for the treatment of bone resorption. Pamidronate-loaded PLGA powders were prepared by means of phys. mixing and spray drying with the control of formulation factors and characterized by scanning electron microscope and X-ray diffractometer. The pamidronate-loaded PLGA powders fabricated into wafers by direct compression under the constant pressure and time at room temperature. These wafers were also observed for their structural characteristic, release pattern, and degradation pattern. The release rate of pamidronate increased with increasing their initial loading ratio as well as increasing wafer thickness. The mol. weight of PLGA affects the release pattern: the higher mol. weight of PLGA, the faster release rate. It can be explained that the higher viscosity of high mol. PLGA solution at same concentration tends to aggregate PLGA and pamidronate resulting in unstable pharmaceutical dosage form. This system had advantages in terms of simplicity in design and obviousness of drug release rate and may be useful as an implantable dosage form for the treatment of aural cholesteatoma.  
 IT 40391-99-9 57248-88-1, Pamidronate disodium  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation and characterization of pamidronate-loaded PLGA wafer for treatment of bone resorption)  
 RN 40391-99-9 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, (9CI) (CA INDEX NAME)



RN 57248-88-1 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI)  
 (CA INDEX NAME)



● 2 Na

on STN  
 ACCESSION NUMBER: 2002163708 EMBASE  
 TITLE: Venlafaxine-associated vaginal bleeding.  
 AUTHOR: Linnebur S.A.; Saseen J.J.; Pace W.D.  
 CORPORATE SOURCE: S.A. Linnebur, Univ. of Colorado Hlth. Sci. Center, Department of Pharmacy Practice, School of Pharmacy, 4200 East Ninth Avenue, Denver, CO 80262, United States. sunny.linnebur@uchsc.edu  
 SOURCE: Pharmacotherapy, (2002) 22/5 (652-655).  
 Refs: 10  
 ISSN: 0277-0008 CODEN: PHPYDQ  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 010 Obstetrics and Gynecology  
 032 Psychiatry  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 039 Pharmacy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB A 41-year-old amenorrheic woman started taking venlafaxine 37.5 mg/day for treatment of depression; 7 days later, she experienced vaginal bleeding, which ceased 1 day after she stopped taking the drug. On rechallenge with venlafaxine, she again experienced vaginal bleeding that resolved after discontinuation. We found no published reports describing vaginal bleeding associated with venlafaxine. However, premarketing and postmarketing data report similar adverse effects in patients taking the agent. In addition, several cases of menstrual irregularities have occurred with two other anti-depressants: fluoxetine and bupropion. This case report supports previous surveillance data indicating that venlafaxine may cause vaginal bleeding.

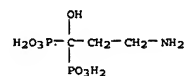
L24 ANSWER 42 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 ACCESSION NUMBER: 2002437234 EMBASE  
 TITLE: Analgesia issues in palliative care: Bone pain, controlled release opioids, managing opioid-induced constipation and nifedipine as an analgesic.  
 AUTHOR: Fine P.G.  
 CORPORATE SOURCE: Dr. P.G. Fine, Department of Anesthesiology, School of Medicine, University of Utah, 50 North Medical Drive, Salt Lake City, UT 84142, United States. fine@arcs.net  
 SOURCE: Journal of Pain and Palliative Care Pharmacotherapy, (2002) 16/1 (93-97).  
 Refs: 4  
 ISSN: 1536-0288 CODEN: JPPCBG  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 016 Cancer  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 039 Pharmacy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Some recent literature relevant to analgesia in palliative care is reviewed. Reports on clinical use of bisphosphonates for bone pain in cancer, controlled release opioids, selection of laxatives for opioid-induced constipation and the calcium channel blocker nifedipine as an analgesic are described. COPYRIGHT. 2002 by The Haworth Press, Inc. All rights reserved.

L24 ANSWER 43 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2001:833023 HCAPLUS  
 DOCUMENT NUMBER: 135:376738  
 TITLE: Compounds and methods for modulating cerebral amyloid angiopathy using inhibitors of an amyloid  $\beta$  peptide  
 INVENTOR(S): Green, Allan M.; Gervais, Francine  
 PATENT ASSIGNEE(S): Neurochem, Inc., Can.  
 SOURCE: PCT Int. Appl., 68 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

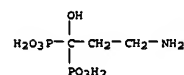
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085093	A2	20011115	WO 2000-1B2078	2001222
WO 2001085093	A3	20020829		
WO 2001085093	C2	20020926		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CH, CA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2395314	AA	20011115	CA 2000-2395314	2001222
AU 2001084313	A5	20011120	AU 2001-84313	2001222
EP 1251837	A2	20021030	EP 2000-993855	2001222
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2000016652	A	20021119	BR 2000-16652	2001222
US 2003003141	A1	20030102	US 2000-747408	2001222
US 6670399	B2	20031230		
JP 2003532656	T2	20031105	JP 2001-581748	2001222
PRIORITY APPLN. INFO.:			US 1999-171877P	P 19991223
			WO 2000-1B2078	W 2001222

OTHER SOURCE(S): MARPAT 135:376738  
 AB The invention provides methods of inhibiting cerebral amyloid angiopathy (CAA) and treating a disease state characterized by cerebral amyloid angiopathy, e.g., Alzheimer's disease, in a subject using an inhibitor of the 39-40 amino acid amyloid  $\beta$  peptide (A $\beta$ 40). The A $\beta$ 40 inhibitor is selected from, e.g., sulfonic acid derivs., such as ethanesulfonic acid, 1,2-ethanedithiosulfonic acid, 1-propanesulfonic acid, 1,3-propanedisulfonic acid, 1,4-butanedisulfonic acid, 1,5-pentanedithiosulfonic acid, 2-aminoethanesulfonic acid, 4-hydroxy-1-butanedisulfonic acid, 1-butanedisulfonic acid, 1-decanedisulfonic acid, 2-propanedisulfonic acid, 3-pentanedithiosulfonic acid, 4-heptanedithiosulfonic acid, etc., and pharmaceutically acceptable salts thereof or from phosphonic acid derivs., such as diethylphosphonoacetic acid, phenylphosphonic acid, 3-aminopropylphosphonic acid, propylphosphonic acid, etc. The compds. are formulated in a dispersion system, a liposome formulation, or microspheres using a polymeric matrix. The polymeric matrix is selected from natural polymers, such as albumin, alginate, cellulose derivs., collagen, fibrin, gelatin, and polysaccharides, or

L24 ANSWER 43 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
 synthetic polymers such as polyesters, polyethylene glycol, poloxamers, and polyanhydrides. For example, the ability of compds. of the invention to inhibit CAA was measured in 9 wk old hAPP transgenic mice treated with two different concns. of a compd. of the present invention, 3-amino-1-propanesulfonic acid sodium salt, 100 and 30 mg/kg. Mice were administered the compd. for 8 wk, after which they were sacrificed and their brains were perfused and processed for histol. staining with Thioflavin S. This method may also be used as a screening method for detg. activity of a candidate compd. for inhibiting CAA. The extent of CAA in brain sections obtained from these animals was qual. detd. following staining. The results indicate that the test compd. was effective in (i) reducing the no. of mice showing CAA, and (ii) showing an effect on the severity of the deposition seen in the brain vasculature of these animals.  
 IT 40391-99-9 91357-22-1 129318-43-0  
 373645-11-5  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);  
 USES  
 (Uses)  
 (inhibitors of amyloid  $\beta$  peptide for modulating cerebral amyloid angiopathy)  
 RN 40391-99-9 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)



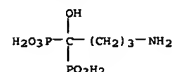
RN 91357-22-1 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, tetrasodium salt (9CI) (CA INDEX NAME)



● 4 Na

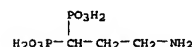
RN 129318-43-0 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI) (CA INDEX NAME)

L24 ANSWER 43 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

RN 373645-11-5 HCAPLUS  
 CN Phosphonic acid, (3-aminopropylidene)bis-, tetrasodium salt (9CI) (CA INDEX NAME)



● 4 Na

L24 ANSWER 44 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2001:780683 HCAPLUS  
 DOCUMENT NUMBER: 135:335156  
 TITLE: Modified-release formulations containing a hypnotic agent  
 INVENTOR(S): Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan  
 PATENT ASSIGNEE(S): Marijn; Van Dalen, Frans; Lemmens, Jacques Maria  
 SOURCE: Synthon B.V., Neth.  
 PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078725	A2	20011025	WO 2001-NL299	20010412
WO 2001078725	A3	20011220		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001050661	A5	20011030	AU 2001-50661	20010412
EP 1272181	A2	20030108	EP 2001-923989	20010412
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2003054041	A1	20030320	US 2001-833662	20010413
US 6638535	B2	20031028		
US 2004047908	A1	20040311	US 2003-657075	20030909
PRIORITY APPL. INFO.:			US 2000-196939P	P 20000413
			WO 2001-NL299	W 20010412
			US 2001-833662	A3 20010413

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

L24 ANSWER 45 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2001:396644 HCAPLUS  
 DOCUMENT NUMBER: 135:24671  
 TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions  
 INVENTOR(S): Patel, Manesh V.; Chen, Peng-jing  
 PATENT ASSIGNEE(S): Lipocine, Inc., USA  
 SOURCE: PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 12  
 PATENT INFORMATION:

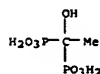
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6248363	B1	20010619	US 1999-447690	19991123
CA 2391923	AA	20010531	CA 2000-2391923	20001122
EP 1233756	A1	20020828	EP 2000-980761	20001122
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003517470	T2	20030527	JP 2001-539423	20001122
PRIORITY APPL. INFO.:			US 1999-447690	A 19991123
			WO 2000-US32255	W 20001122

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A composition contained glyburide 1, PEG 40 stearate 33, glycerol monoleurate 17, and nonpareil seed 80 g.

IT 7414-83-7, Disodium etidronate 37248-88-1, Pamidronate disodium 66376-36-1, Alendronate 89987-06-4, Tiludronate 105462-24-6, Risedronic acid  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

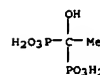
L24 ANSWER 44 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)

IT 2809-21-4  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (modified-release formulations containing hypnotic agent)  
 RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



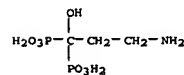
L24 ANSWER 45 OF 79 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)

RN 7414-83-7 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



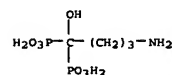
● 2 Na

RN 57248-88-1 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

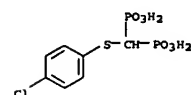


● 2 Na

RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

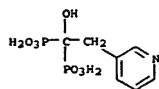


RN 89987-06-4 HCAPLUS  
 CN Phosphonic acid, [(4-chlorophenyl)thio)methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS

L24 ANSWER 45 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
CN Phosphonic acid, (1-hydroxy-2-(3-pyridinyl)ethylidene)bis- (9CI) (CA INDEX NAME)



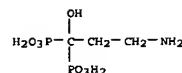
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L24 ANSWER 46 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:265229 HCAPLUS  
DOCUMENT NUMBER: 134:285588  
TITLE: Pharmaceutical formulation for menopausal women comprising fatty acids, calcium compounds, and folic acid  
INVENTOR(S): Levinson, R. Saul; Hermelin, Marc S.; Kirschner, Mitchell I.  
PATENT ASSIGNEE(S): KV Pharmaceutical Company, USA  
SOURCE: PCT Int. Appl., 88 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

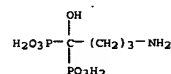
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024772	A1	20010412	WO 2000-US23527	20000828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6479545	B1	20021112	US 1999-409059	19990930
CA 2385854	AA	20010412	CA 2000-2185854	20000828
EP 1216024	A1	20020626	EP 2000-957857	20000828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000014438	A	20020820	BR 2000-14438	20000828
JP 2003510344	T2	20030318	JP 2001-527771	20000828
AU 778507	B2	20041209	AU 2000-69416	20000828
US 2002137749	A1	20020926	US 2002-106381	20020327
ZA 2002002633	A	20020225	ZA 2002-2633	20020404
US 2002173510	A1	20021121	US 2002-131236	20020425
PRIORITY APPLN. INFO.:			US 1999-409059	A 19990930
			WO 2000-US23527	W 20000828

AB The present disclosure relates to novel compns. which provide improved nutritional support for premenopausal and menopausal women and/or relief from symptoms associated with menopause, as well as prophylactic effects, and methods for using same. A pharmaceutical composition contained vitamin A 5000, vitamin D 400, vitamin E 400 IU, vitamin C 100, vitamin B1 20, vitamin B2 20, vitamin B6 25, vitamin B12 50, vitamin B3 100, folic acid 1.0, calcium carbonate 1200, copper 2, zinc 15, DHA/linolenic/linoleic acid 50/25/25 mg, and selenium 65 µg.  
IT 40391-99-9 66376-36-1, Alendronate 89987-06-4, Tiludronate 105462-24-6, Risedronic acid  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical formulation for menopausal women comprising fatty acids, calcium compds., and folic acid)  
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

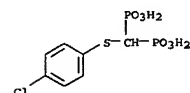
L24 ANSWER 46 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



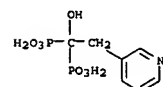
RN 66376-36-1 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [(4-chlorophenylthio)methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [(1-hydroxy-2-(3-pyridinyl)ethylidene)bis- (9CI) (CA INDEX NAME)



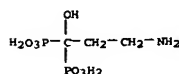
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L24 ANSWER 47 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:136991 HCAPLUS  
DOCUMENT NUMBER: 134:198075  
TITLE: Triglyceride-free compositions and methods for enhanced absorption of hydrophilic therapeutic agents  
INVENTOR(S): Patel, Mahesh V.; Chen, Feng-Jing  
PATENT ASSIGNEE(S): Lipocine, Inc., USA  
SOURCE: PCT Int. Appl., 113 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 12  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012155	A1	20010222	WO 2000-US18807	20000710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6309663	B1	20011030	US 1999-375636	19990817
CA 2380642	AA	20010222	CA 2000-2380642	20000710
EP 1210063	A1	20020605	EP 2000-947184	20000710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506476	T2	20030218	JP 2001-516502	20000710
NZ 517659	A	20041224	NZ 2000-517659	20000710
US 2001024658	A1	20010927	US 2000-751968	20001229
US 6458383	B2	20021001		
PRIORITY APPLN. INFO.:			US 1999-375636	A 19990817
			WO 2000-US18807	W 20000710

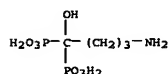
AB The present invention relates to triglyceride-free pharmaceutical compns., pharmaceutical systems, and methods for enhanced absorption of hydrophilic therapeutic agents. The compns. and systems include an absorption enhancing carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. A hydrophilic therapeutic agent can be incorporated into the composition, or can be co-administered with the composition as part of a pharmaceutical system. The invention also provides methods of treatment with hydrophilic therapeutic agents using these compns. and systems. For example, when a composition containing Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18, and propylene glycol 0.32 g, resp., was used, the relative absorption of PEG 4000 as a model macromol. drug was enhanced by 991%.  
IT 37248-99-1, Panidronate disodium 66376-36-1, Alendronate 89987-06-4, Tiludronate 105462-24-6, Risedronic acid  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

L24 ANSWER 47 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
 RN 57248-88-1 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

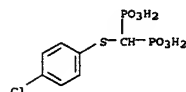


● 2 Na

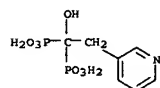
RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)



RN 89987-06-4 HCAPLUS  
 CN Phosphonic acid, [[[4-chlorophenyl]thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 105462-24-6 HCAPLUS  
 CN Phosphonic acid, (1-hydroxy-2-(3-pyridinylethylidene)bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RECORD.

FORMAT

L24 ANSWER 49 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
 ACCESSION NUMBER: 2001227030 EMBASE  
 TITLE: Pathogenesis and pharmacological treatment of bone pain in skeletal metastases.  
 AUTHOR: Ripamonti C.; Fulfaro F.  
 CORPORATE SOURCE: C. Ripamonti, Rehab. Pain Therapy/Palliative Care, National Cancer Institute, Via Venezian 1, 20133 Milan, Italy.  
 SOURCE: ripamonti@istitutotumori.mi.it  
 (65-77). Quarterly Journal of Nuclear Medicine, (2001) 45/1

Refs: 119  
 ISSN: 1124-3937 CODEN: QJNMF7  
 Italy -  
 COUNTRY: Italy  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 016 Cancer  
 008 Neurology and Neurosurgery  
 038 Adverse Reactions Titles  
 037 Drug Literature Index  
 030 Pharmacology  
 014 Radiology  
 005 General Pathology and Pathological Anatomy  
 023 Nuclear Medicine  
 036 Health Policy, Economics and Management

LANGUAGE: English  
 SUMMARY LANGUAGE: English

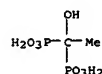
AB Sixty-five percent of patients with advanced cancer present bone metastases and most of them present a rather slow clinical course characterized by pain, mobility deficiencies and skeletal complications such as fractures and spinal cord compression. Metastatic involvement of the bone is one of the most frequent causes of pain in cancer patients and represents one of the first signs of widespread neoplastic disease. The pain may originate directly from the bone, from nerve root compression or from muscle spasms in the area of the lesions. The mechanisms of metastatic bone pain is mainly somatic (nociceptive) even though, in some cases, neuropathic and visceral stimulations may overlap. The conventional symptomatic treatment of metastatic bone pain requires the use of multidisciplinary therapies such as radiotherapy in association with systemic treatment (hormonotherapy, chemotherapy, radioisotopes) with the support of analgesic therapy. Recently, studies have indicated the use of bisphosphonates in the treatment of pain and in the prevention of skeletal complications in patients with metastatic bone disease. In some patients pharmacological treatment, radiotherapy, radioisotopes administered alone or in association are not able to manage pain adequately. The role of neuroinvasive techniques in treating metastatic bone pain is debated. The clinical conditions of the patient, his life expectancy and quality of life must guide the physician in the choice of the best possible therapy.

L24 ANSWER 48 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2001:396514 HCAPLUS  
 DOCUMENT NUMBER: 135:7194  
 TITLE: Detergent composition with controlled release of its components  
 INVENTOR(S): Schmiedel, Peter; Gassenmeier, Thomas Otto; Von Rybinski, Wolfgang; Kesseler, Arnd; Hardacker, Ingo; Speckmann, Horst-Dieter; Poethkow, Jorg; Krupp, Ute  
 PATENT ASSIGNEE(S): Henkel Kommanditgesellschaft auf Aktien, Germany  
 SOURCE: Eur. Pat. Appl., 20 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1103594	A2	20010530	EP 2000-125074	20001117
EP 1103594	A3	20031015		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO  
 PRIORITY APPLN. INFO.: DE 1999-19957038 A 19991126

OTHER SOURCE(S): MARPAT 135:7194  
 AB Solid detergent composition with improved soil/stain removal capability, especially with bleachable soils and at lower washing temps., comprises an alkalinizing agent, e.g., alkali carbonate, Na tripolyphosphate, etc., which is released to the washing liquor at a controlled rate. The alkalinizing agent is encapsulated or compounded in such a way that 50% of the agent is released after t1 of 1-25 min and 250% is released after t1 + 3-25 min of the washing process.  
 IT 29329-71-3, Sodium 1-hydroxyethane-1,1-diphosphonate  
 RL: TEM (Technical or engineered material use); USES (Uses) (solid detergent composition with controlled release of alkalinizing agents)  
 RN 29329-71-3 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis-, sodium salt (9CI) (CA INDEX NAME)



● x Na

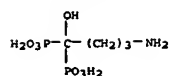
L24 ANSWER 50 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2000:608556 HCAPLUS  
 DOCUMENT NUMBER: 133:198679  
 TITLE: Solid oral dosage form containing a permeation enhancer  
 INVENTOR(S): Cumming, Kenneth Iain; Ramcoola, Zebunnissa  
 PATENT ASSIGNEE(S): Elan Corporation, P.L.C., Ire.  
 SOURCE: PCT Int. Appl., 65 pp.  
 CODEN: PIXX22  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050012	A1	20000831	WO 2000-GB628	20000222

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2363123 A1 20000831 CA 2000-2363123 20000222  
 EP 1154761 A1 20011121 EP 2000-905186 20000222  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO  
 JP 2002537321 T2 20021105 JP 2000-600624 20000222  
 US 2003091623 A1 20030515 US 2000-510560 20000222  
 PRIORITY APPLN. INFO.: US 1999-121048P P 19990222  
 WO 2000-GB628 W 20000222

AB The invention relates to a solid oral dosage form comprising a pharmaceutically active ingredient in combination with a permeation enhancer which enhances the bioavailability and/or the absorption of the active ingredient. Accordingly, a solid oral dosage form comprises a drug and an permeation enhancer wherein the enhancer is a medium chain fatty acid ester, ether or salt or a derivative of a medium chain fatty acid, which is, preferably, solid at room temperature and which has a carbon chain length of from 6 to 20 carbon atoms. Preferably, the solid oral dosage form is a controlled-release dosage form such as a delayed-release dosage form. The effect of sodium salts of various medium chain fatty acid on the transport of TSH releasing hormone across cultured Caco-2 cells was studied. Immediate-release tablets containing leuprolide 0.05, sodium caprate 68.82, silica 0.5, magnesium stearate 0.5, lactose 20, and disintegrant 8% were prepared  
 IT 66376-36-1, Alendronate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (solid oral dosage form containing permeation enhancer)  
 RN 66376-36-1 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 50 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L24 ANSWER 51 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:259972 HCAPLUS  
DOCUMENT NUMBER: 132:293042  
TITLE: Encapsulation of sensitive liquid components into a matrix to obtain discrete shelf-stable particles  
INVENTOR(S): Van Lengerich, Bernhard H.  
PATENT ASSIGNEE(S): General Mills, Inc., USA  
SOURCE: PCT Int. Appl., 56 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

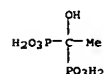
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021504	A1	20000420	WO 1999-US20905	19991006
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, CZ, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, CA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2345815	AA	20000420	CA 1999-2345815	19991006
AU 9963872	A1	20000501	AU 1999-63872	19991006
AU 777977	B2	20041104		
EP 1119345	A1	20010801	EP 1999-951433	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527375	T2	20020827	JP 2000-575480	19991006
PRIORITY APPLM. INFO.:				
			US 1998-103700P	P 19981009
			US 1998-109696P	P 19981124
			US 1999-233443	A 19990120
			WO 1999-US20905	W 19991006

AB A liquid encapsulant component which contains an active, sensitive encapsulant, such as a live microorganism or an enzyme dissolved or dispersed in a liquid plasticizer is admixed with a plasticizable matrix material. The matrix material is plasticizable by the liquid plasticizer and the encapsulation of the active encapsulant is accomplished at a low temperature and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous process to produce discrete, solid particles. The liquid content of the liquid encapsulant component provides substantially all or completely all of the liquid plasticizer needed to plasticize the matrix component to obtain a formable, extrudable, cuttable, mixture or dough. Removal of liquid plasticizer prior to extrusion is not needed to adjust the viscosity of the mixture for formability. Release of an active component from the matrix may be delayed or controlled over time so that the active component is delivered when and where it is needed to perform its intended function. Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component

L24 ANSWER 51 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant.  
IT 7414-83-7, Etidronate disodium  
RL: FPD (Food or feed use); BIOL (Biological study); USES (Uses) (encapsulation of sensitive liquid components into matrix to obtain discrete shelf-stable particles)

RN 7414-83-7 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L24 ANSWER 52 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

ON STN  
ACCESSION NUMBER: 2000354618 EMBASE  
TITLE: Perioperative considerations in patients with metastatic bone disease.  
AUTHOR: Bibbo C.; Patel D.V.; Benevenia J.  
CORPORATE SOURCE: C. Bibbo, 2840 Thornbush Court, Charlotte, NC 28270.  
United States  
SOURCE: Orthopedic Clinics of North America, (2000) 31/4 (577-595).  
Refs: 102  
ISSN: 0030-5898 CODEN: OCLNAQ  
United States  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 016 Cancer  
019 Rehabilitation and Physical Medicine  
033 Orthopedic Surgery  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Preoperative assessment of patients with metastatic bone disease includes a history and physical examination, laboratory evaluation, and standard radiographs. Perioperative diagnostics include technetium bone scan, CT scans, MR imaging, positron emission tomography, and biopsy. The role of preoperative tumor embolization and vena cava filter placement is discussed in this article. Guidelines for pain control are provided. Surgical planning and instrument considerations for long bone lesions, peritumoral lesions, and pelvis and acetabular lesions are addressed. The importance of rehabilitation for patients with metastatic bone disease is emphasized.

L24 ANSWER 53 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:219978 HCAPLUS  
 DOCUMENT NUMBER: 130:242329  
 TITLE: Solid solution beadlet comprising a long chain fatty acid or ester, a surfactant  
 INVENTOR(S): Burnside, Beth A.; McGuinness, Charlotte M.; Rudnic, Edward M.; Couch, Richard A.; Guo, Xiaodi; Tustian, Alexander K.  
 PATENT ASSIGNEE(S): Shire Laboratories, Inc., USA  
 SOURCE: PCT Int. Appl., 69 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913864	A2	19990325	WO 1998-US19658	19980918
WO 9913864	A3	19990812		
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2302275	AA	19990325	CA 1998-2302275	19980918
AU 8894967	A1	19990405	AU 1998-94967	19980918
EP 1028712	A2	20000823	EP 1998-948383	19980918
EP 1028712	B1	20050112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2001006650	A1	20010705	US 1998-156464	19980918
US 6692767	B2	20040217		
JP 2002522354	T2	20020723	JP 2000-511488	19980918
AT 286721	E	20050115	AT 1998-948383	19980918
PRIORITY APPLN. INFO.:			US 1997-59408P	P 19970919
			WO 1998-US19658	W 19980918

AB Disclosed is a beadlet comprising (i) a hydrophobic long chain fatty acid or ester material; (ii) a surfactant; and (iii) a therapeutic agent, which in admixt. form a solid solution at room temperature. The hydrophobic material preferably has a m.p. of about 40 to about 100°, and is most preferably glyceryl behenate. The surfactant is preferably a polyglycolized glyceride, polyoxyethylene sorbate, ethylene or propylene block copolymer or combinations thereof, and is most preferably polyoxyethylene 20 sorbitan monolaurate. Uncoated beadlets were prepared containing acyclovir (i) 35, Iabrazol 20, Compritol 888 40, Calc 58. The transport of 1 through Caco-2 cell monolayers was 18.0 times the control.

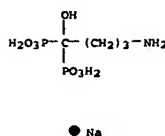
IT 129318-43-0, Alendronate sodium  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (solid solution beadlet comprising long chain fatty acid or ester surfactant)

RN 129318-43-0 HCAPLUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI)  
 (CA INDEX NAME)

L24 ANSWER 54 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 ACCESSION NUMBER: 1999152202 EMBASE  
 TITLE: Trends in cancer pain management.  
 AUTHOR: Lesage P.; Portenoy R.K.  
 CORPORATE SOURCE: Dr. R.K. Portenoy, Pain Medicine/Palliative Care Dept., Beth Israel Medical Center, First Avenue at 16th Street, New York, NY 10003, United States  
 SOURCE: Cancer Control, (1999) 6/2 (136-145).  
 Refs: 36  
 ISSN: 1073-2748 CODEN: CACOFD  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 016 Cancer  
 023 Nuclear Medicine  
 024 Anesthesiology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Background: Pain is a prevalent symptom in cancer patients, affecting up to 50% of patients undergoing active cancer treatment and up to 90% of those with advanced disease. Although adequate relief can be achieved in the majority of cancer patients, pain is often treated inadequately in traditional settings. Methods: The authors use their experience and that of others to review the evaluation and diagnosis of pain syndromes and the principles of management. Results: The World Health Organization and other governmental agencies have recognized the importance of pain management as part of routine cancer care. Conducting a comprehensive assessment, competently providing analgesic drugs, and communicating with the patient and family allow effective management of pain in the cancer patients. Conclusions: Several approaches can promote adequate management of cancer pain, such as enhancing clinician knowledge of pain syndromes, improving pain assessment, and updating medical information related to pain and symptom control.

L24 ANSWER 53 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

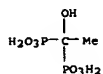


L24 ANSWER 55 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1998:293427 HCAPLUS  
 DOCUMENT NUMBER: 129:8597  
 TITLE: Embedding and encapsulation of controlled release particles  
 INVENTOR(S): Van Lengerich, Bernhard H.  
 PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA  
 SOURCE: PCT Int. Appl., 63 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818610	A1	19980507	WO 1997-US18984	19971027
W: AU, CA, JP, NO, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2269806	AA	19980507	CA 1997-2269806	19971027
AU 9749915	A1	19980522	AU 1997-49915	19971027
AU 744156	B2	20020214		
EP 935523	A1	19990818	EP 1997-912825	19971027
EP 935523	B1	20040929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511777	T2	20020416	JP 1998-520558	19971027
EP 1342548	A1	20030910	EP 2003-10031	19971027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 277739	E	20041015	AT 1997-912825	19971027
NO 9902036	A	19990428	NO 1999-2036	19990428
PRIORITY APPLN. INFO.:			US 1996-29038P	P 19961028
			US 1997-52717P	P 19970716
			EP 1997-912825	A3 19971027
			WO 1997-US18984	W 19971027

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced.

L24 ANSWER 55 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
prior to admixing the plasticized mass with the encapsulant to avoid  
substantial destruction of the encapsulant and to obtain a formable,  
extrudable mixt. The mixt. is extruded through a die without substantial  
or essentially no expansion and cut into discrete, relatively dense  
particles. Release properties may also be controlled  
by precoating the encapsulant and/or coating the extruded particles with  
a film-forming component. An example of encapsulation of acetylcysteine is  
given using starch, polyethylene, glycerol monostearate, and vegetable  
oil.  
IT 7414-83-7, Etidronate disodium  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
use); BIOL (Biological study); PROC (Process); USES (Uses)  
(embedding and encapsulation of controlled release  
particles)  
RN 7414-83-7 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA  
INDEX NAME)



● 2 Na

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

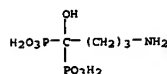
L24 ANSWER 56 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS  
RESERVED.  
on STN  
ACCESSION NUMBER: 97263326 EMBASE  
DOCUMENT NUMBER: 1997263326  
TITLE: Risedronate Sodium.  
SOURCE: Drugs of the Future, (1997) 22/7 (799).  
Refs: 2  
ISSN: 0377-8282 CODEN: DRFUD4  
Spain  
COUNTRY: Journal; (Short Survey)  
DOCUMENT TYPE: 029 Clinical Biochemistry  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1997105205 HCAPLUS  
DOCUMENT NUMBER: 126122508  
TITLE: Bisphosphonate cement composition to prevent  
aseptic loosening of orthopedic implant devices  
INVENTOR(S): Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.  
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Simpson, Hamish; Athanasou,  
Nick; Yates, Ashley J.  
SOURCE: PCT Int. Appl., 20 pp.  
CODEN: PIXXDA  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639107	A1	19961212	WO 1996-US8515	19960603
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, DE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
RW: KE, LA, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2223450	AA	19961212	CA 1996-2223450	19960603
EP 831756	A1	19980401	EP 1996-917041	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11511041	T2	19990928	JP 1996-501089	19960603
PRIORITY APPLN. INFO.:			US 1995-470404	A 19960603
			WO 1996-US8515	W 19960603

AB Disclosed is a bisphosphonate bone cement for preventing peri-prosthetic  
bone loss and aseptic loosening of a joint prosthesis in patients, which  
cement contains a bisphosphonate bone resorption inhibitor, e.g. Na or Ca  
salt of alendronate and a pharmaceutically acceptable  
polymeric carrier such as poly(Me methacrylate). A  
composition containing Me methacrylate, N,N-dimethyl-p-toluidine, and  
chlorophyll was added to a composition containing Me methacrylate-Me  
acrylate copolymer, benzoyl peroxide, ZrO<sub>2</sub>, chlorophyll, and gentamicin,  
then alendronate Na was added to give a cement mixture  
IT 185959-98-2P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(bone implant cements containing bisphosphonate bone resorption  
inhibitor  
and polymeric carrier)  
RN 185959-98-2 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt,  
monohydrate (9CI) (CA INDEX NAME)

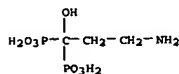
L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



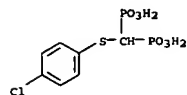
● 2 Na

● H<sub>2</sub>O

IT 40391-99-9 89987-06-4, Tiludronic acid  
105462-24-6 129318-43-0, Alendronate sodium  
137504-89-3 157432-53-6 186090-69-7  
186090-70-0  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(bone implant cements containing bisphosphonate bone resorption  
inhibitor and polymeric carrier)  
RN 40391-99-9 HCAPLUS  
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX  
NAME)

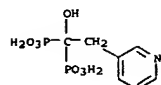


RN 89987-06-4 HCAPLUS  
CN Phosphonic acid, [(4-chlorophenyl)thio]methylene]bis- (9CI) (CA INDEX  
NAME)

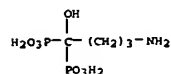


RN 105462-24-6 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA  
INDEX NAME)

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

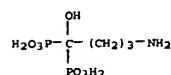


RN 129318-43-0 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt (9CI)  
(CA INDEX NAME)



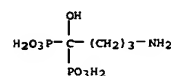
● Na

RN 137504-89-3 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (1:1)  
(9CI) (CA INDEX NAME)



● Ca

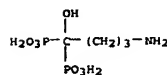
RN 157432-53-6 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, magnesium salt (9CI)  
(CA INDEX NAME)



● x Mg

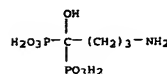
RN 186090-69-7 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, barium salt (9CI)  
(CA INDEX NAME)

L24 ANSWER 57 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
INDEX NAME



● x Ba

RN 186090-70-0 HCAPLUS  
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt (2:3)  
(9CI) (CA INDEX NAME)



● 3/2 Na

L24 ANSWER 58 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:504204 HCAPLUS  
DOCUMENT NUMBER: 125:151223  
TITLE: Bioabsorbable ceramic implants for bone repair  
INVENTOR(S): Irie, Hiroyuki  
PATENT ASSIGNEE(S): Olympus Optical Co, Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.  
CODEN: JXXXXF

DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

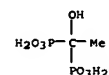
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08141067	A2	19960604	JP 1994-282035	19941116
JP 3476930	B2	20031210		

PRIORITY APPLN. INFO.: JP 1994-282035 19941116

AB The bioabsorbable ceramic implants comprise porous  $\beta$ -tricalcium phosphate block and sustained-release bone resorption-inhibiting drug (1-hydroxyethylidene-1,1-diphosphonic acid). The ceramic implants are useful for bone repair.

IT 2809-21-4, 1-Hydroxyethylidene-1,1-diphosphonic acid  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(bioabsorbable ceramic implants for bone repair)

RN 2809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 59 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 96189161 EMBASE  
DOCUMENT NUMBER: 1996189161  
TITLE: Endocrinology.  
AUTHOR: Watts N.B.; Blevins Jr. L.S.  
CORPORATE SOURCE: Emory University School of Medicine, Atlanta, GA, United States  
SOURCE: Journal of the American Medical Association, (1996) 275/23 (1806-1807).  
ISSN: 0098-7484 CODEN: JAMAAP  
COUNTRY: United States  
DOCUMENT TYPE: Journal; (Short Survey)  
FILE SEGMENT: 003 Endocrinology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English

on STN  
 ACCESSION NUMBER: 96247146 EMBASE  
 DOCUMENT NUMBER: 1996247146  
 TITLE: Osteoporosis: The need for comprehensive treatment guidelines.  
 AUTHOR: Abbott III T.A.; Lawrence B.J.; Wallach S.  
 CORPORATE SOURCE: Pharmacoconomics, Sandoz Pharmaceuticals Corporation, 59 Route 10, East Hanover, NJ 07936-1080, United States  
 SOURCE: Clinical Therapeutics, (1996) 18/1 (127-149).  
 ISSN: 0149-2918 CODEN: CLTHDG  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 003 Endocrinology  
 019 Rehabilitation and Physical Medicine  
 020 Gerontology and Geriatrics  
 033 Orthopedic Surgery  
 036 Health Policy, Economics and Management  
 030 Pharmacology  
 037 Drug Literature Index

LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Osteoporosis is a debilitating disease that results in nearly 1.3 million fractures per year in the United States. The cost of treating these fractures has been estimated to be as high as \$10 billion per year. These costs are expected to more than double during the next 50 years unless comprehensive programs of prevention and treatment are initiated. Both pharmacologic and nonpharmacologic interventions (eg, diet and exercise) have been shown to have a significant impact on the incidence

of osteoporosis, depending on the time of their application. Unfortunately, osteoporosis is often not diagnosed until after fractures have occurred, when it may be too late for treatment to have a major impact. To be most effective, therapy should be started early, before serious bone loss has occurred. Because of its efficacy and relatively low acquisition cost, long-term hormone replacement therapy (HRT) is considered first-line pharmacologic therapy for the prevention of osteoporosis. However, for various reasons, less than 25% of US women who might benefit from HRT are receiving it. Aside from HRT, the only other products approved by the US Food and Drug Administration for the treatment of osteoporosis are salmon calcitonin and alendronate. Several other agents are under development, including sustained-release fluoride and other products in the bisphosphonate class. The development and adoption of early detection programs and treatment guidelines are crucial to help ease the economic burden of osteoporosis. These guidelines should incorporate preventive measures such as diet and exercise, risk

assessment through proper screening programs, and the appropriate use of pharmaceutical products. The purpose of this paper is to discuss relevant economic issues associated with osteoporosis and discuss the need for a management algorithm that could be used to more efficiently prevent and treat this disease. We conclude that further modeling is needed to determine which programs and treatments are most cost-effective within each at-risk subgroup. As clinicians better understand the need for preventive care and the advantages of the various pharmacologic therapies, patients with osteoporosis will receive higher-quality and more efficient medical care.

on STN  
 ACCESSION NUMBER: 96014247 EMBASE  
 DOCUMENT NUMBER: 1996014247  
 TITLE: New drugs for osteoporosis.  
 SOURCE: Medical Letter on Drugs and Therapeutics, (1996) 38/965 (1-3).  
 ISSN: 0025-732X CODEN: MELEAP  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 003 Endocrinology  
 010 Obstetrics and Gynecology  
 033 Orthopedic Surgery  
 036 Health Policy, Economics and Management  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English

ACCESSION NUMBER: 1996-161211 HCAPLUS  
 DOCUMENT NUMBER: 124:185591  
 TITLE: Controlled-release oral drug delivery forms containing hydrogel-forming polymers  
 PATENT ASSIGNEE(S): Yissum Research Development Co., Israel  
 SOURCE: PCT Int. Appl., 35 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

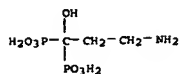
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534294	A1	19951221	WO 1995-US7519	19950613
W: AM, AT, AU, BB, BR, BY, CA, CH, CN, CZ, DE, DK, FI, GB, HU, JP, KP, RO, RU, SD, SE				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, ES, FR, GB, IT, LU, MC, SE, BF, BJ, MR, NE, SN, TD, TG				
IL 110024	A1	19980405	IL 1994-110024	19940615
AU 9528270	A1	19960105	AU 1995-28270	19950613
US 6692766	B1	20040217	US 1997-750674	19970228
US 2004185107	A1	20040923	US 2003-630918	20030731
US 2004219216	A1	20041104	US 2003-630917	20030731
PRIORITY APPLN. INFO.:			IL 1994-110024	A 19940615
			WO 1995-US7519	W 19950613
			US 1997-750674	A1 19970228

AB The present invention relates to a controlled-release drug delivery system comprising a drug which is susceptible to enzymic degradation by enzymes present in the intestinal tract and a polymeric matrix. The polymeric matrix which undergoes erosion in the gastrointestinal tract comprises a hydrogel-forming polymer selected from the group consisting of (a) polymers which are themselves capable of enhancing absorption of the drug across the intestinal mucosal tissues and of inhibiting degradation of the drug by intestinal enzymes and (b) polymers which are not themselves capable of enhancing absorption of the drug across the intestinal mucosal tissues and of inhibiting degradation of the drug by intestinal enzymes. The delivery system optionally further comprises an agent which enhances absorption of the drug across the intestinal mucosal tissues and/or an agent which inhibits degradation of the drug by intestinal enzymes. For example, bradykinin was incubated with 0.5% polycarboxophil suspension, then  $\alpha$ -chymotrypsin was added to the mixture and the incubation proceeded for addnl. 120 min. Almost no degradation of bradykinin was detected.

IT 40391-99-9  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (controlled-release oral formulations containing polymeric matrix for drugs susceptible to enzymic degradation)

RN 40391-99-9 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

L24 ANSWER 62 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L24 ANSWER 63 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:554875 HCAPLUS  
DOCUMENT NUMBER: 123:40904

TITLE: Synergism of calcium ethanehydroxybisphosphonate (CaEHP) and FeCl<sub>3</sub>: controlled release polymers for preventing calcification of bioprosthetic aortic wall

AUTHOR(S): Vyavahare, Narendra R.; Ou, Xuan; Lee, Michael; Behari, Priya; Schoen, Frederick J.; Levy, Robert J.  
CORPORATE SOURCE: Department of Pediatrics and Communicable Diseases, Kresge II, Room 5014, P.O.B. 0576, University of Michigan Medical School, Ann Arbor, MI, 48109-0576, USA

SOURCE: Journal of Controlled Release (1995), 34(2), 97-108  
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

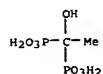
AB Controlled release delivery implants based on ethylene-vinyl acetate (EVA) copolymer were studied for prevention of calcification of aortic wall in an intracirculatory rat allograft model. The calcium salt of ethanehydroxybisphosphonate (CaEHP) and ferric chloride (FeCl<sub>3</sub>) were used as anti-calcification drugs either in combination or sep. in solvent-cast EVA films. These matrixes were characterized in vitro for their drug release at 37°C at pH 7.4 (0.05 M HEPES buffer). Inulin was included in the single drug loaded systems as an inert filler to obtain comparable loadings. The films released the drugs in vitro continuously over 60 days without any rapid burst phase. For rat allograft studies controlled release matrixes or non-drug EVA films were sutured periadventitially to the aortic wall allografts to study the anticalcification efficacy for 30 days. The calcium and phosphorous levels of the explanted allografts were quantified. Controlled release films releasing both the drugs (CaEHP and FeCl<sub>3</sub>) together synergistically inhibited calcification of the aortic walls. CaEHP alone releasing from EVA polymer was partially effective, and EVA films releasing only FeCl<sub>3</sub> did not inhibit calcification at all. Overall, no adverse effects on somatic growth or recipient bone morphol. were noted following controlled release drug administration.

IT 75323-71-6  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)  
(synergism of calcium ethanehydroxybisphosphonate and FeCl<sub>3</sub>: controlled release polymers for preventing calcification of bioprosthetic aortic wall)

RN 75323-71-6 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis-, calcium salt (9CI) (CA INDEX NAME)

L24 ANSWER 63 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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on STN  
ACCESSION NUMBER: 96002869 EMBASE  
DOCUMENT NUMBER: 1996002869

TITLE: Palliative care: Cancer pain management.  
AUTHOR: Glare P.  
CORPORATE SOURCE: Dept. of Medical Oncology/Pall. Care, Westmead Hospital, Westmead, NSW, Australia  
SOURCE: Modern Medicine of Australia, (1995) 38/12 (36-51).  
ISSN: 1030-3782 CODEN: MMAUB7

COUNTRY: Australia  
DOCUMENT TYPE: Journal; (Short Survey)  
FILE SEGMENT: 006 Internal Medicine  
008 Neurology and Neurosurgery  
016 Cancer  
024 Anesthesiology  
048 Gastroenterology  
017 Drug Literature Index

LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Intractable pain should no longer be feared as the inevitable consequence of advanced cancer. For the vast majority of patients, cancer pain can be controlled by following a four-point approach based on correct assessment of the pain mechanisms and the patient's psychological state. Reducing

the noxious stimulus and attending to psychosocial problems are the cornerstones of the treatment plan. Sometimes opioid analgesics like morphine are also required. Not all types of pain responds well to opioids, and adjuvant analgesic drugs are then required. Techniques such as nerve blocks and surgery have a place in selected cases.

Practicalities of each of these aspects are discussed in this article.

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on STN  
ACCESSION NUMBER: 94113826 EMBASE  
DOCUMENT NUMBER: 1994113826  
TITLE: Slow-release sodium fluoride in the management of postmenopausal osteoporosis: A randomized controlled trial.  
AUTHOR: Pak C.Y.C.; Sakhaee K.; Piziak V.; Peterson R.D.; Breslau N.A.; Boyd P.; Poindexter J.R.; Herzog J.; Heard-Sakhaee A.; Haynes S.; Adams-Huet B.; Reisch J.S.  
CORPORATE SOURCE: Texas Southwestern Med. Ctr. Univ., 5323 Harry Hines Boulevard, Dallas, TX 75235-8885, United States  
SOURCE: Annals of Internal Medicine. (1994) 120/8 (625-632). ISSN: 0003-4819 CODEN: AIMEAS  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 003 Endocrinology  
006 Internal Medicine  
033 Orthopedic Surgery  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Objective: To test whether intermittent treatment with slow-release sodium fluoride and continuous calcium citrate supplementation inhibits vertebral fractures without causing fluoride complications. Design: A placebo-controlled, randomized trial. Setting: Outpatient setting of specialty clinics in Dallas and Temple, Texas. Interventions: Slow-release sodium fluoride (25 mg twice daily) in repeated 14-month cycles (12 months on treatment followed by 2 months off treatment) compared with placebo. Both groups took calcium citrate (400 mg calcium twice daily) continuously. Patients: 110 patients with postmenopausal osteoporosis were randomly assigned to two groups. In the slow-release sodium fluoride group, 48 of 54 patients completed more than 1 cycle of treatment (mean, 2.44 cycles/patient), whereas 51 of 56 patients in the placebo group completed at least 1 cycle (mean, 2.14 cycles/patient) in this interim analysis. Measurements: Vertebral fracture rate and lumbar bone mineral content. Vertebral fractures were quantified from yearly radiographs. Bone mass was determined annually by densitometry. Results: In the sodium fluoride group, the mean L2 to L4 bone mineral content increased by 4% to 6% in each cycle and the mean femoral neck bone density increased by 4.1% and 2.1% during the first two cycles, but the radial bone density did not change. The placebo group showed no statistical change in bone mass at any site. Compared with the placebo group, the sodium fluoride group had a lower individual new vertebral fracture rate (0.057/patient cycle compared with 0.204/patient cycle, P = 0.017), a higher fracture-free rate (83.3% compared with 64.7%, P = 0.042), and a lower group fracture rate (0.085/patient cycle compared with 0.239/patient cycle, P = 0.006). The side-effect profile was similar for the two groups; no patient developed microfractures, hip fractures, or blood loss anemia. Conclusions: Intermittent slow-release sodium fluoride plus continuous calcium citrate, administered for about 2.5 years, inhibits new vertebral fractures, increases the mean spinal bone mass without decreasing the radial shaft

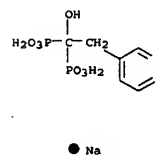
L24 ANSWER 65 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. (Continued)  
bone density, and is safe to use.

L24 ANSWER 66 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:434350 HCAPLUS  
DOCUMENT NUMBER: 119:34350  
TITLE: Risedronate enteric-coated sustained-release compositions  
INVENTOR(S): Danesereau, Richard John; Mosher, Russell Youker; Axelrod, Douglas Wayne; Sietsema, William Kendall  
PATENT ASSIGNEE(S): Procter and Gamble Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 34 pp. CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9109785	A1	19930527	WO 1992-US9385	19921102
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9230604	A1	19930615	AU 1992-30604	19921102
AU 661080	B2	19950713		
EP 613373	A1	19940907	EP 1992-924208	19921102
EP 613373	B1	20000802		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
JP 07501073	T2	19950202	JP 1993-509287	19921102
HU 67681	A2	19950428	HU 1994-1357	19921102
BR 9206797	A	19951031	BR 1992-6797	19921102
CZ 282760	B6	19970917	CZ 1994-1230	19921102
CA 2122479	C	19980825	CA 1992-2122479	19921102
RU 2120798	C1	19981027	RU 1994-27277	19921102
SK 279589	B6	19990111	SK 1994-595	19921102
AT 195075	E	20000815	AT 1992-924208	19921102
ES 2149781	T3	20001116	ES 1992-924208	19921102
ZA 9303337	A	19931118	ZA 1993-3337	19930513
IL 105714	A1	19970610	IL 1993-105714	19930517
FI 9402366	A	19940520	FI 1994-2366	19940520
FI 113240	B1	20040321		
NO 9401894	A	19940719	NO 1994-1894	19940520
US 5622721	A	19970422	US 1994-307495	19940914
US 5935602	A	19990810	US 1997-820430	19970312
US 6096342	A	20000801	US 1999-303466	19990430
US 6596710	B1	20030722	US 2000-591911	20000609
GR 3034373	T3	20001229	GR 2000-402060	20000908
US 2004037884	A1	20040226	US 2003-455880	20030606
PRIORITY APPLN. INFO.:			US 1991-796151	A 19911122

L24 ANSWER 66 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
of risedronate are disclosed. The dosage forms protect the epithelial and mucosal tissues of the buccal cavity, pharynx, esophagus, and stomach from irritation and deliver the drug to the lower intestinal tract of the mammal. Round-shaped tablets contg. 30 mg risedronic acid Na were coated with a coating suspension contg. Eudragit L30D 33.400, PEG 1.000, talc 2.500, yellow iron oxide 0.034, simethicone emulsion 0.800, and water 75.000 mg to obtain enteric-coated sustained-release tablets.  
IT 115436-72-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceuticals containing, enteric-coated and sustained-release)  
RN 115436-72-1 HCAPLUS  
CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt (9CI) (CA INDEX NAME)



AB Oral enteric-coated and sustained-release dosage forms

Searched by: Mary Hale 571-272-2507 REM 1D86

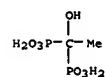
L24 ANSWER 67 OF 79 MEDLINE on STN DUPLICATE 2  
 ACCESSION NUMBER: 94002882 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 8399967  
 TITLE: Synergistic inhibition of the calcification of glutaraldehyde pretreated bovine pericardium in a rat subdermal model by FeCl3 and ethanedihydroxydiphosphonate: preincubation and polymeric controlled release studies.  
 AUTHOR: Hirach D; Drader J; Pathak Y V; Yee R; Schoen F J; Levy R J  
 CORPORATE SOURCE: Department of Pediatrics, University of Michigan Medical School, Ann Arbor 48109-0576.  
 CONTRACT NUMBER: HL 38118 (NHLBI)  
 SOURCE: Biomaterials, (1993 Jul) 14 (9) 705-11.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article: (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199311  
 ENTRY DATE: Entered STN: 19940117  
 Last Updated on STN: 19940117  
 Entered Medline: 19931124

AB Calcification is a frequent cause of the clinical failure of bioprosthetic heart valves fabricated from glutaraldehyde-pretreated porcine aortic valves or glutaraldehyde-pretreated bovine pericardium (GPBP). We investigated the hypothesis that ferric chloride (FeCl3) and sodium-ethanedihydroxydiphosphonate (EHDP) may act synergistically to prevent bioprosthetic tissue calcification. Pre-incubations and controlled release systems were studied individually. FeCl3-EHDP polymeric controlled release matrices were formulated using silicone rubber and evaluated for in vitro release kinetics at pH 7.4 and 37 degrees C. The effects of Fe-EHDP synergism on GPBP calcification were investigated with 21 d subdermal implants in 3 wk-old male rats. Results demonstrated that levels of Fe3+ and EHDP uptake, measured in GPBP tissues pre-incubated first in an FeCl3 solution (10(-5) M) followed by an EHDP solution (0.1 M), were higher than in the reverse order of incubation. In the first series of rat implants, GPBP was pre-incubated in either FeCl3 or Na2EHDP solutions, or sequential pre-incubations of first FeCl3 and then Na2EHDP solutions, or the reverse. The inhibition of calcification was greatest when FeCl3 (first pre-incubation, 10(-5) M) was combined with Na2EHDP (second pre-incubation, 0.1 M) (1.78 +/- 0.2 micrograms of Ca2+/mg of dried tissue) compared with the other pre-incubation groups: EHDP (first pre-incubation) combined with FeCl3 (second pre-incubation) (21.7 +/- 6.4), FeCl3 solution alone at 10(-5) M (27.9 +/- 10.7), Na2EHDP solution alone at 0.1 M (52.3 +/- 11.9) and the control group (72.3 +/- 10.2). In a second series of implants, GPBP specimens were co-implanted with individual controlled release systems containing one of the following formulations (weight percentage in silicone rubber): 1% FeCl3, 20% CaEHDP, 20% protamine sulphate, 1% FeCl3-20% CaEHDP, and 1% FeCl3-20% protamine sulphate. The 1% FeCl3-20% CaEHDP silicone-rubber matrices were the most effective for inhibiting GPBP mineralization (13.7 +/- 3.0 micrograms Ca2+/mg of dried tissue) compared with non-drug silicone co-implant controls (74.7 +/- 5.58 micrograms Ca2+/mg of dried tissue) and other polymeric treatment groups (32.3 +/- 2.3-80.0 +/- 19.7). No adverse effects on bone or overall growth of any treatment protocols

L24 ANSWER 67 OF 79 MEDLINE on STN DUPLICATE 2  
 (Continued)  
 were noted. Thus, combinations of FeCl3 and EHDP, using either pre-incubations or polymeric controlled release, were synergistic for inhibiting GPBP calcification.

L24 ANSWER 68 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:546496 HCAPLUS  
 DOCUMENT NUMBER: 119:146496  
 TITLE: Site-specific delivery of ethanedihydroxy diphosphonate from refillable polyurethane reservoirs to inhibit bioprosthetic tissue calcification  
 AUTHOR(S): Johnston, T. P.; Webb, C. L.; Schoen, F. J.; Levy, R. J.  
 CORPORATE SOURCE: Coll. Pharm., Univ. Illinois, Chicago, IL, USA  
 SOURCE: Journal of Controlled Release (1993), 25(3), 227-40  
 CODEN: JCRREC; ISSN: 0168-3659  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Calcification (CALC) is the most frequent cause for the failure of bioprosthetic heart valves fabricated from glutaraldehyde-pretreated porcine aortic valve, and contributes to the failure of glutaraldehyde pretreated bovine pericardial (BNV) bioprosthetic heart valves as well. Although systemic therapy in rats using ethanedihydroxy diphosphonate (EHDP) has proven successful in inhibiting CALC, adverse effects on serum calcium, bone development, and overall somatic growth have been noted. The present study was designed to evaluate the potential of site-specific delivery of EHDP to arrest CALC of glutaraldehyde-pretreated bovine pericardium when implanted subdermally in rats using a refillable reservoir drug delivery device. The refillable reservoir devices evaluated in these studies exhibited constant (zero-order) release of EHDP in vitro and replenishment of the drug supply when implanted subdermally in rats was achieved in a noninvasive fashion using an exteriorized entrance and exit cannula. The refillable reservoirs evaluated were fabricated from a com. available polyurethane (Biomer). Glutaraldehyde-pretreated bovine pericardium was implanted subdermally in 21-day-old rats either alone (control) or with refillable Biomer reservoirs with (treatment) or without (sham) a 2 M solution of Na2EHDP. Implanted reservoirs which initially contained a 2 M solution of Na2EHDP were refilled with a fresh 2 M solution of Na2EHDP on days 7 and 14 post-initial surgery using a syringe and the exteriorized entrance and exit cannulas. Pericardium retrieved following 21 days and assayed for calcium showed significant inhibition in CALC for tissue implanted adjacent to refillable Biomer reservoirs containing EHDP (6.9 µg/mg) compared to control (179.0 ± 13.5 µg/mg) and sham-implanted (152.0 ± 10.2 µg/mg) rats. Unimplanted pericardium had a mean tissue calcium concentration of 3.0 ± 0.5 µg/mg. Based on the in vitro release studies of EHDP from refillable Biomer reservoirs, the estimated dose delivered when implanted subdermally in rats in the present study was 5.5 ± 0.7 mg/kg per day. For rats implanted with EHDP-containing refillable reservoirs, histol. examination of retrieved pericardium and femurs from rats in each group confirmed both complete inhibition of CALC of the glutaraldehyde crosslinked pericardium and no untoward effects on bone development, resp. In addition, blood samples obtained at sacrifice showed no change in serum Ca2+ concns. in EHDP-treated animals compared to controls. Thus, the site-specific delivery of EHDP using refillable Biomer reservoirs was successful for inhibiting BNV CALC in a rat subdermal model with no untoward effects on bone development, serum Ca2+ concns., or overall growth. The advantages

L24 ANSWER 68 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
 of the refillable reservoir system are its const. (zero-order) rate of EHDP release and its potential for replenishment of EHDP by noninvasive means when the EHDP soln. inside the reservoir has been depleted.  
 IT 2809-21-4  
 RL: BIOL (Biological study)  
 (controlled and site-specific delivery of, from refillable polyurethane reservoirs for inhibiting bioprosthetic heart valve calcification)  
 RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 69 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 ACCESSION NUMBER: 93269535 EMBASE  
 DOCUMENT NUMBER: 1993269535  
 TITLE: Controlled release diphosphonate  
 adventitial implants for prevention of aortic valve  
 allograft calcifications.  
 AUTHOR: Qu X.; Trachy J.; Jurva J.; Underwood T.; Levy R.J.  
 CORPORATE SOURCE: Univ of Michigan Medical School, Ann Arbor, MI 48109-0576,  
 United States  
 SOURCE: Proceedings of the Controlled Release Society, (1993) -/20  
 (125-126).  
 CODEN: 58GM4H  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Conference Article  
 FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English

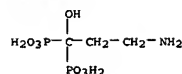
L24 ANSWER 70 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 ACCESSION NUMBER: 93072251 EMBASE  
 DOCUMENT NUMBER: 1993072251  
 TITLE: [Myths about dihydrocodiene as an analgesic in cancer  
 pain].  
 AUTHOR: NOCH IMMER 'BLUMEN' FALSCHER VORURTEILE. DIHYDROCODEIN ALS  
 KREBS-SCHMERZBREMSER.  
 CORPORATE SOURCE: Ilias W.  
 Abteilung für Anaesthesie, Krankenhaus der Barmherzigen  
 Brüder, Grosse Mohrengasse 9, A-1020 Wien, Austria  
 SOURCE: Therapiewoche Österreich, (1993) 8/2 (97-98-100).  
 ISSN: 0258-848X CODEN: THOEE6  
 COUNTRY: Austria  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 016 Cancer  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: German  
 SUMMARY LANGUAGE: English; German

L24 ANSWER 71 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1991:520060 HCAPLUS  
 DOCUMENT NUMBER: 115:120060  
 TITLE: Disodium pamidronate double-coated granules  
 INVENTOR(S): Wirth, Dagmar; Bucher, Christian  
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.  
 SOURCE: Can. Pat. Appl., 16 pp.  
 CODEN: CPXMEB  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2024631	AA	19910308	CA 1990-2024631	19900905
CA 2024631	C	20001121		
EP 421921	A1	19910410	EP 1990-810661	19900830
EP 421921	B1	19940427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 104856	E	19940515	AT 1990-810661	19900830
ES 2052228	T3	19940701	ES 1990-810661	19900830
IL 95558	A1	19950831	IL 1990-95558	19900831
FI 93169	B	19941130	FI 1990-4341	19900903
FI 93169	C	19950310		
US 5096717	A	19920317	US 1990-577420	19900904
DD 298049	A5	19920206	DD 1990-343841	19900905
NO 9003892	A	19910308	NO 1990-3892	19900906
NO 176646	B	19950130		
NO 176646	C	19950510		
AU 9062283	A1	19910314	AU 1990-62283	19900906
AU 623036	B2	19920430		
JP 03099016	A2	19910424	JP 1990-234618	19900906
JP 1009713	B2	20000214		
ZA 9007100	A	19910529	ZA 1990-7100	19900906
HU 59008	A2	19920428	HU 1990-5812	19900906
HU 207447	B	19930428		
PRIORITY APPLN. INFO.:				
			CH 1989-3245	A 19890907
			EP 1990-810661	A 19900830

AB A controlled-release granule comprises di-Na  
 pamidronate.5H<sub>2</sub>O (I) which is coated with a hydrophilic, elastic inner  
 coating and a gastric juice-resistant intestinal juice-soluble outer  
 coating.  
 Controlled-release granule core pellets contained I  
 197.3, Avicel PH105 52.7 mg/each; inner coating contained cellulose HP-M  
 603 10.0, polyethylene glycol 2.0, and talc 8.0 mg/each; and outer  
 coating  
 contained Eudragit L30D 90.0, tri-Et citrate 21.0, Antifoam AP 2.0, and  
 talc 7.0 mg/each.  
 IT 109552-15-0  
 RL: BIOL (Biological study)  
 (controlled-release pharmaceutical  
 granules containing)  
 RN 109552-15-0 HCAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt,  
 pentahydrate (9CI) (CA INDEX NAME)

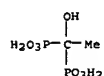
L24 ANSWER 71 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



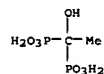
● 2 Na

● 5 H<sub>2</sub>O

L24 ANSWER 72 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1992:181009 HCAPLUS  
 DOCUMENT NUMBER: 116:181009  
 TITLE: Characterization and anticalcification effects of implantable polyurethane matrices containing amorphous dispersion of bisphosphonic acid  
 AUTHOR(S): Golomb, Gershon; Wagner, David  
 CORPORATE SOURCE: Sch. Pharm., Hebrew Univ., Jerusalem, 91120, Israel  
 SOURCE: Clinical Materials (1991), 8(1-2), 33-42  
 CODEN: CLMME2; ISSN: 0267-6605  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Cardiovascular calcification, the formation of calcium phosphate deposits in cardiovascular tissue, is a common-end stage phenomenon affecting a wide variety of cardiovascular disease states and causing the dysfunction of many different types of biomaterial implants. The present investigation describes the formulation, characterization, and the in-vivo efficacy of prolonged controlled-release polyurethane matrices containing the anticalcification agent 1,1-hydroxyethylidene bisphosphonic acid (HEBP). Sustained-release polyurethane (PU) matrices with amorphous dispersion of the drug, in its free acid form, were obtained. Matrices morphol. and release kinetics were solvent and concentration dependent. All HEBP matrices (co-implanted subdermally in rats with the calcifiable bioprosthetic heart valve tissue) significantly inhibited tissue calcification (76.3 µg/mg Ca<sup>2+</sup> in comparison to 1.1-10.1 µg/mg Ca<sup>2+</sup>, untreated and treated groups, resp.). Systemic side effects were noted only in the rats implanted with the 10% weight/weight HEBP matrices. It is concluded that PU matrices with amorphous dispersion of HEBP provided effective and sustained anticalcification properties.  
 IT 2809-21-4  
 RL: BIOL (Biological study)  
 (anticalcification effects and controlled release of, from polyurethane implants)  
 RN 2809-21-4 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis-, (9CI) (CA INDEX NAME)



L24 ANSWER 73 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1990:412041 HCAPLUS  
 DOCUMENT NUMBER: 113:12041  
 TITLE: Controlled-release implants for cardiovascular disease  
 AUTHOR(S): Levy, Robert J.; Johnston, Thomas P.; Sintov, Amnon; Golomb, Gershon  
 CORPORATE SOURCE: Div. Pediatr. Cardiol., C.S. Mott Child. Hosp., Ann Arbor, MI, 48109, USA  
 SOURCE: Journal of Controlled Release (1990), 11(1-3), 245-54  
 CODEN: JCREEC; ISSN: 0168-3659  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The systemic therapy of many cardiovascular diseases is often hampered by adverse drug effects. The use of controlled-release implants as a means for optimizing drug concns. at the affected site and in the cardiovascular system, while using a relatively low systemic dose, was examined. Controlled-release systems were prepared by combining a drug of choice with either a non-degradable polymer, such as silicone rubber, polyurethane, and ethylene vinylacetate, or a biodegradable compound such as poly(glycolic-lactic acid) or a high-mol.-weight polyanhydride. Controlled-release matrices containing ethylenedihydroxydiphosphonate (EHDP), when implanted next to a bioprosthetic heart valve leaflet, prevented pathol. calcification. Similarly, controlled-release matrices containing lidocaine-HCl were used exptl. as epicardial implants to convert ventricular tachycardia to normal sinus rhythm in dogs. Future controlled-release systems for cardiovascular use will very likely incorporate innovative design features including: a reservoir configuration to replenish or change drug therapy, modulatable drug release to vary drug dosing as desired, and closed-loop feedback to increase or decrease release rates in response to disease status.  
 IT 7414-83-7  
 RL: BIOL (Biological study)  
 (polymer implants for controlled-release of, for cardiovascular disease treatment)  
 RN 7414-83-7 HCAPLUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

L24 ANSWER 74 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN DUPLICATE 3  
 ACCESSION NUMBER: 90089191 EMBASE  
 DOCUMENT NUMBER: 1990089191  
 TITLE: Controlled release of ethanehydroxy diphosphonate from polyurethane reservoirs to inhibit calcification of bovine pericardium used in bioprosthetic heart valves.  
 AUTHOR: Johnston T.P.; Boyd J.A.; Ciesliga B.L.; Schoen F.J.; Amidon G.; Levy R.J.  
 CORPORATE SOURCE: Department of Pediatrics and Communicable Disease, University of Michigan, Ann Arbor, MI 48109, United States  
 SOURCE: International Journal of Pharmaceutics, (1990) 59/2 (95-104).  
 ISSN: 0378-5173 CODEN: IJPHDE  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Calcification (CALC) of bioprosthetic heart valves (BHVs) fabricated from either glutaraldehyde-pretreated bovine pericardial tissue or porcine aortic valves is the most frequent cause of clinical failure of these devices. Previous studies have demonstrated that calcification is inhibited by diphosphonate compounds released into the vicinity of bioprosthetic tissue implanted subcutaneously in rats. Controlled release of the anticalcification agent ethanehydroxy diphosphonate (EHDP), as a 1:1 mixture of Na<sub>2</sub>EHDP and CaEHDP from cylindrical polyurethane (PU) reservoirs (o.d. = 0.36 cm, i.d. = 0.33 cm, length = 4 cm) fabricated by solvent casting was assessed in vitro and in vivo. The diffusivity (D), determined independently using standard diffusion cells, for ionic EHDP diffusion across the PU membrane was 1.2 x 10<sup>-10</sup> cm<sup>2</sup>/s. Volume influx of buffer into the reservoirs in vitro was observed experimentally to reach a maximum at 7.8 days (288 ± 44 µl) with a biexponential decline to 147 ± 6 µl at 70 days. The cumulative EHDP released in vitro after 70 days was 4.2 ± 0.6% (4.8 ± 0.7 mg) compared to 15.7 ± 3.2% (16.1 ± 3.7 mg) in vivo (subcutaneously in 3 week-old, male, CD rats) over 21 days. The release rate of EHDP from the reservoirs was not a zero-order process. Reservoir administration of EHDP effectively inhibited pericardial BHV-CALC in 21-day subdermal explants (Ca<sup>2+</sup> = 4.5 ± 1.4 µg Ca<sup>2+</sup>/mg tissue; control, Ca<sup>2+</sup> = 120 ± 13 µg Ca<sup>2+</sup>/mg tissue) without diphosphonate-related untoward effects at a dose of approx. 3 mg/kg per day.

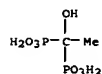
L24 ANSWER 75 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN DUPLICATE 4  
 ACCESSION NUMBER: 89148836 EMBASE  
 DOCUMENT NUMBER: 1989148836  
 TITLE: Controlled release of 1-hydroxyethylidene diphosphonate: In vitro assessment and effects on bioprosthetic calcification in sheep tricuspid valve replacements.  
 AUTHOR: Johnston T.P.; Bove E.L.; Bolling S.F.; Boyd J.A.; Ciesliga B.L.; Amidon G.L.; Schoen F.J.; Levy R.J.  
 CORPORATE SOURCE: Department of Pediatrics and Communicable Disease, C.S. Mott Children's Hospital, University of Michigan Medical Center, Ann Arbor, MI 48109-0576, United States  
 SOURCE: International Journal of Pharmaceutics, (1989) 52/2 (139-148).  
 ISSN: 0378-5173 CODEN: IJPHDE  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal  
 FILE SEGMENT: 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Calcification (CALC) is the most frequent cause of the clinical failure of bioprosthetic valves (BHVs). Controlled-release (paravalvar) administration of the anticalcification agent ethanehydroxydiphosphonate (EHDP), as either Na<sub>2</sub>EHDP or in combination (1:1) with the less soluble CaEHDP, from a silicone rubber matrix (20% w/w EHDP) was studied both in vitro and in vivo for the prevention of BHV CALC. Seventeen sheep (6-7 months old, male, Suffolk) underwent tricuspid valve replacement using Hancock I, 25 mm porcine aortic bioprostheses. explant evaluation after 16-20 weeks revealed that two of the 7 control BHV were calcified (139 ± 20.8 µg Ca<sup>2+</sup>/mg of tissue), while none of the 9 BHV retrieved from animals receiving controlled release EHDP demonstrated CALC (4.41 ± 1.09 µg Ca<sup>2+</sup>/mg of tissue). No adverse effects of EHDP on bone or calcium metabolism were noted. The cumulative percent of EHDP released per electron microprobe analysis was 40.4% ± 9.68 (Na, CaEHDP) to 79.0% ± 4.82 (Na<sub>2</sub>EHDP) in vivo compared to 35.7% ± 7.72 and 78.6 ± 11.1 in vitro, respectively. Assessment of the Young's modulus (Y) using thermomechanical analysis (TMA) revealed a 1.5-fold (Silastic Q7-4840) to 9.5-fold (Silastic 382) increase in Y following drug loading. The Y for explanted, Silastic Q7-4840 polymer matrices ranged from 2.84 x 10<sup>4</sup> to 5.57 x 10<sup>5</sup> dyne/cm<sup>2</sup>. In vitro osmotic related matrix swelling of the Na<sub>2</sub>EHDP loaded, unsealed matrices (20% w/w) after 75 days was minimized to a 35.8% increase in weight due to incorporation of CaEHDP with Na<sub>2</sub>EHDP in a 1:1 ratio and was further reduced (22.2% increase in weight) by sealing 76% of the releasing surface, compared to Na<sub>2</sub>EHDP matrices which demonstrated a 414% and 141% increase in weight, respectively.

L24 ANSWER 76 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 88270653 EMBASE  
DOCUMENT NUMBER: 1988270653  
TITLE: Local controlled release of 1-hydroxyethylidene diphosphonate using silicone-rubber matrices. Effects of sterilization on in vitro release and in vivo efficacy.  
AUTHOR: Johnston T.P.; Bove E.L.; Bolling S.F.; Schoen F.J.; Boyd J.A.; Golomb G.; Levy R.J.  
CORPORATE SOURCE: Department of Pediatrics and Communicable Diseases, Division of Pediatric Cardiology, C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI  
48109-0576.  
United States  
SOURCE: ASAIO Transactions, (1988) 34/3 (835-838).  
ISSN: 0889-7190 CODEN: ASATEJ  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
019 Rehabilitation and Physical Medicine  
027 Biophysics, Bioengineering and Medical Instrumentation  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Calcification (CALC) is the most frequent cause of the clinical failure of bioprosthetic heart valves (BHVs). Controlled release of disodium ethanehydroxydiphosphonate (EHDP) has been demonstrated to inhibit subdermal BHV calcification at effective low local doses, avoiding adverse effects. However, the eventual circulatory use of controlled release EHDP necessitates addressing several critical issues that may affect efficacy. These include the effects of sterilization on EHDP release and the efficacy of sustained release matrices containing CaEHDP, which is less soluble than NaEHDP. The effects of CaEHDP-NaEHDP incorporation and steam sterilization on controlled release of EHDP from silicone-rubber matrices was studied both in vitro and in vivo using a rat subdermal model and sheep tricuspid valve replacements. Autoclaved EHDP matrices (20% wt/wt) released  $88.9\% \pm 7.84$  of contained drug after 140 days in vitro, compared with control ( $87.6\% \pm 10.3$  cumulative release). Autoclaved EHDP matrices completely inhibited BHV CALC in 60 day rat subdermal implants ( $8.84 \pm 3.68$   $\mu\text{g Ca}^{++}/\text{mg tissue}$ ), comparable to nonsterilized EHDP-loaded matrices ( $7.06 \pm 2.00$   $\mu\text{g Ca}^{++}/\text{mg tissue}$ ). Nontreated CALC levels were  $183 \pm 7.60$   $\mu\text{g Ca}^{++}/\text{mg tissue}$ . Na-CaEHDP co-incorporation into silicone rubber matrices markedly prolonged controlled release with the 1:1 Na-CaEHDP mixture demonstrating an extrapolated release duration of approximately 20 years, assuming the total amount of dispersed drug was released. Data from tricuspid valve replacements in sheep demonstrate erratic control calcification ( $41.3 \pm 14.9$   $\mu\text{g Ca}^{++}/\text{mg tissue}$ ), but complete suppression of BHV calcification with Na2EHDP controlled release ( $5.74 \pm 1.35$   $\mu\text{g Ca}^{++}/\text{mg tissue}$ ) after 150 days.

L24 ANSWER 77 OF 79 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:498604 HCAPLUS  
DOCUMENT NUMBER: 109:98604  
TITLE: Controlled release of diphosphonates from synthetic polymers to inhibit calcification  
AUTHOR(S): Golomb, Gershon  
CORPORATE SOURCE: Sch. Pharm., Hebrew Univ. Jerusalem, Jerusalem, 91120, Israel  
SOURCE: Journal of Biomaterials Applications (1987), 2(2), 266-89  
CODEN: JBAPEL; ISSN: 0885-3282  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review with 39 refs. on formulation and evaluation of controlled release drug delivery system for diphosphonates to inhibit bioprosthetic heart valve calcification.  
IT 2809-21-4D, 1-Hydroxyethanediphosphonic acid, derivs.  
RL: PROC (Process)  
(controlled release of, from polymers, for inhibition of calcification of bioprosthetic heart valves)  
RN 2809-21-4 HCAPLUS  
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)



L24 ANSWER 76 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. (Continued)

L24 ANSWER 78 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 87036698 EMBASE  
DOCUMENT NUMBER: 1987036698  
TITLE: Controlled release of diphosphonate to inhibit bioprosthetic heart valve calcification: Dose-response and mechanistic studies.  
AUTHOR: Golomb G.; Langer R.; Schoen F.J.; et al.  
CORPORATE SOURCE: Department of Pediatrics, Harvard Medical School, Boston, MA 02115, United States  
SOURCE: Journal of Controlled Release, (1986) 4/3 (181-194).  
CODEN: JCREEC  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index  
030 Pharmacology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
LANGUAGE: English

L24 ANSWER 79 OF 79 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN  
ACCESSION NUMBER: 85192958 EMBASE  
DOCUMENT NUMBER: 1985192958  
TITLE: Bioefficient products. A novel delivery system.  
AUTHOR: Tossounian J.L.; Mergens W.J.; Sheth P.R.  
CORPORATE SOURCE: Pharmacy R & D, Hoffmann-La Roche, Nutley, NJ 07110, United States

SOURCE: States  
Drug Development and Industrial Pharmacy, (1985) 11/5  
(1019-1050).  
CODEN: DDIPDH  
COUNTRY: United States

DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index  
030 Pharmacology  
048 Gastroenterology

LANGUAGE: English

AB Studies have shown that a bioefficient/HBS(TM) dosage form is more bioavailable than the conventional product. This is true with compounds which are absorbed from the upper portion of the small intestine or intended to act in the stomach contents. The increase in bioavailability is due to the design of this delivery system which is based on the HBS(TM)

having a prolonged retention in the stomach, as shown by scintillation studies. Vitamins evaluated in these experiments include riboflavin, thiamine and a vitamin C plus E combination product.

L25 0 FILE MEDLINE  
L26 0 FILE BIOSIS  
L27 0 FILE EMBASE  
L28 1 FILE HCAPLUS

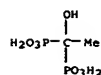
TOTAL FOR ALL FILES  
L29 1 LS AND (DASCH J7/AU OR RILEY M7/AU)

L29 ANSWER 1 OF 1 HCAPIUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:813899 HCAPIUS  
 DOCUMENT NUMBER: 137:299972  
 TITLE: Modification of the sustained-release profile of a drug by a biocompatible polymer and a bisphosphonate  
 INVENTOR(S): Dasch, James R.; Riley, M. Gary I.  
 PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA  
 SOURCE: PCT Int. Appl., 49 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

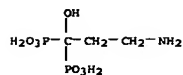
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083096	A1	20021024	WO 2002-US8440	20020319
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TR				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004100	A1	20030102	US 2001-835001	20010413
US 6558702	B2	20030506		
CA 2444421	AA	20021024	CA 2002-2444421	20020319
EP 1395240	A1	20040319	EP 2002-709857	20020319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512218	T2	20041021	JP 2002-580900	20020319
US 2003216192	A1	20031225	US 2003-400162	20030325
US 2004147488	A1	20040729	US 2004-758717	20040116
PRIORITY APPLN. INFO.: US 2001-835001 A 20010413				
WO 2002-US8440 W 20020319				
US 2003-400162 A1 20030325				

AB The present invention relates to a method for the sustained release in vivo of a biol. active agent comprising administering to a subject in need of treatment an effective amount of a sustained-release composition comprising a biocompatible polymer having the biol. active agent incorporated therein, and a bisphosphonate wherein the bisphosphonate compound is present in an amount sufficient to modify the release profile of the biol. active agent from the sustained-release composition Pharmaceutical compns. suitable for use in the method of the invention are also disclosed.  
 IT 2809-21-4 57248-88-1 66376-36-1, Alendronate  
 89987-06-4, Tiludronate 115436-72-1  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (modification of sustained-release profile of drug by biocompatible polymer and bisphosphonate)  
 RN 2809-21-4 HCAPIUS  
 CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)

L29 ANSWER 1 OF 1 HCAPIUS COPYRIGHT 2005 ACS on STN (Continued)

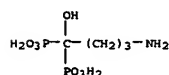


RN 57248-88-1 HCAPIUS  
 CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

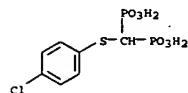


● 2 Na

RN 66376-36-1 HCAPIUS  
 CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

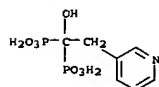


RN 89987-06-4 HCAPIUS  
 CN Phosphonic acid, [[[4-chlorophenyl]thio]methylene]bis- (9CI) (CA INDEX NAME)



RN 115436-72-1 HCAPIUS  
 CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-, monosodium salt (9CI) (CA INDEX NAME)

L29 ANSWER 1 OF 1 HCAPIUS COPYRIGHT 2005 ACS on STN (Continued)



● Na

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

=> s ((sustain? or timed or control?) (4a)releas? or prolonged action) and (polymer? carrier? or poly lactide co glycolide or polygalactin 910 or glycolic lactic acid polyester)

L30 125 FILE MEDLINE  
L31 162 FILE BIOSIS  
L32 188 FILE EMBASE  
L33 522 FILE HCAPLUS

TOTAL FOR ALL FILES

L34 997 ((SUSTAIN? OR TIMED OR CONTROL?) (4A) RELEAS? OR PROLONGED ACTION ) AND (POLYMER? CARRIER? OR POLY LACTIDE CO GLYCOLIDE OR POLYGAL ACTIN 910 OR GLYCOLIC LACTIC ACID POLYESTER)

=> s l34 and (compos? or pharm?)

L35 66 FILE MEDLINE  
L36 154 FILE BIOSIS  
L37 171 FILE EMBASE  
L38 273 FILE HCAPLUS

TOTAL FOR ALL FILES

L39 664 L34 AND (COMPOS? OR PHARM?)

=> s l39 and (dasch j?/au or riley m?/au)

L40 0 FILE MEDLINE  
L41 0 FILE BIOSIS  
L42 1 FILE EMBASE  
L43 0 FILE HCAPLUS

TOTAL FOR ALL FILES

L44 1 L39 AND (DASCH J?/AU OR RILEY M?/AU)

=> s l44 not l29

L45 0 FILE MEDLINE  
L46 0 FILE BIOSIS  
L47 1 FILE EMBASE  
L48 0 FILE HCAPLUS

TOTAL FOR ALL FILES

L49 1 L44 NOT L29

=> d ibib abs

L49 ANSWER 1 OF 1 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
ACCESSION NUMBER: 97241159 EMBASE  
DOCUMENT NUMBER: 1997241159  
TITLE: In-vivo and in-vitro degradation of poly(lactide-co-glycolide) microspheres.  
AUTHOR: Tracy M.A.; Zhang Y.; Verdon S.L.; Dong N.; Riley M.G.I.  
CORPORATE SOURCE: M.A. Tracy, Alkermes Inc, Cambridge, MA 02139, United States  
SOURCE: Proceedings of the Controlled Release Society, (1997) -/24 (623-624).  
Refs: 3  
ISSN: 1022-0178 CODEN: 58GMAH  
COUNTRY: United States  
DOCUMENT TYPE: Journal: Article  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English

=> s (dasch j?/au and riley m?/au)  
L50 0 FILE MEDLINE  
L51 1 FILE BIOSIS  
L52 0 FILE EMBASE  
L53 1 FILE HCAPLUS

TOTAL FOR ALL FILES

L54 2 (DASCH J?/AU AND RILEY M?/AU)

=> s l54 not (l29 or l44)  
L55 0 FILE MEDLINE  
L56 1 FILE BIOSIS  
L57 0 FILE EMBASE  
L58 0 FILE HCAPLUS

TOTAL FOR ALL FILES

L59 1 L54 NOT (L29 OR L44)

=> d ibib abs

L59 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN  
ACCESSION NUMBER: 2003:265994 BIOSIS  
DOCUMENT NUMBER: PREV200300265994  
TITLE: Method of modifying the release profile of sustained  
release compositions.  
AUTHOR(S): Dasch, James R. [Inventor, Reprint Author];  
Riley, M. Gary I. [Inventor]  
CORPORATE SOURCE: Needham, MA, USA  
ASSIGNEE: Alkermes Controlled Therapeutics, Inc.  
PATENT INFORMATION: US 6558702 May 06, 2003  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (May 6 2003) Vol. 1270, No. 1.  
<http://www.uspto.gov/web/menu/patdata.html>, e-file.  
ISSN: 0098-1133 (ISSN print).  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 4 Jun 2003  
Last Updated on STN: 4 Jun 2003  
AB The present invention relates to a method for the sustained release in  
vivo of a biologically active agent comprising administering to a subject  
in need of treatment an effective amount of a sustained release  
composition comprising a biocompatible polymer having the biologically  
active agent incorporated therein, and a bisphosphonate wherein the  
bisphosphonate compound is present in an amount sufficient to modify the  
release profile of the biologically active agent from the sustained  
release composition. Pharmaceutical compositions suitable for use in the  
method of the invention are also disclosed.

=> fil caol;s l3  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
387.29	551.84

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-35.04	-35.04

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COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966  
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L60 10 L3

=> d 1-10

L60 ANSWER 1 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA65:20175f CAOLD  
 TI detergent-impregnated gloves  
 PA Trimex  
 DT Patent  
 TI washing products  
 PA Procter & Gamble Co.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI FR 1432675  
 PI NL 6517236  
 IT 1643-20-5 2666-14-0 13502-12-0 13502-28-8  
 13513-23-0 13529-88-9

L60 ANSWER 2 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA65:13968g CAOLD  
 TI detergent additives (synergistic)  
 PA Procter & Gamble Co.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI NL 6413483  
 IT 2281-11-0 2666-14-0 2809-21-4 7425-12-9  
 13419-36-8

L60 ANSWER 3 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA65:12238d CAOLD  
 TI 1-hydroxyethylidenediphosphonic acid  
 PA Albright & Wilson (Mfg.) Ltd.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI BE 672168  
 NL 6514452  
 IT 2809-21-4 7316-54-3 7414-83-7

L60 ANSWER 4 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA65:5685a CAOLD  
 TI methylenediphosphonic acids (substituted)  
 PA Procter & Gamble Co.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI GB 1026366  
 IT 1660-95-3 4775-92-2 6145-32-0 6145-33-1 10038-58-1  
 10419-56-4 10595-91-2 10595-92-3 10595-93-4 10596-16-4 10596-19-7  
 10596-20-0 10596-21-1 10596-22-2 10596-23-3 10596-24-4 10596-26-6  
 10596-27-7 10596-28-8 10596-29-9 10596-30-2 10596-31-3 10596-32-4  
 13004-12-1 13005-02-2 13040-51-2 13428-84-7  
 13428-85-8

L60 ANSWER 5 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA64:8505b CAOLD  
 TI detergent tablets containing auxiliaries  
 PA Henkel & Cie G.m.b.H.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI BE 650885  
 FR 1408414  
 IT 3794-83-0

L60 ANSWER 6 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA64:8237h CAOLD  
 TI phosphonic acids or their salts  
 PA Henkel & Cie G.m.b.H.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI FR 1412865  
 BE 655066  
 GB 1032378  
 IT 2809-21-4 3794-83-0 4712-07-6 7101-46-4\*\*\*

L60 ANSWER 7 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA64:3862c CAOLD  
 TI chlorine-forming agents with sequestering properties  
 PA Monsanto Co.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI NL 6407365  
 BE 649996  
 FR 1403179  
 GB 1039966  
 IT 87-90-1 1984-15-2 2244-21-5 2782-57-2 2893-78-9 6145-29-5  
 6145-31-9 6145-32-0 \*\*\*6145-33-1 6202-99-9 13840-33-0

L60 ANSWER 8 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA63:9991e CAOLD  
 TI 1-hydroxy-1,1-alkyldiphosphonic acids  
 AU Germscheid, Hans G.  
 PA Henkel & Cie G.m.b.H.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI DE 1194852  
 NL 6410204  
 IT 2666-14-0 2809-18-9 2809-20-3 2809-21-4\*\*\*

L60 ANSWER 9 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA63:4092f CAOLD  
 TI dyeing of human hair  
 PA Oreal S. A.  
 DT Patent  
 TI reduction of damage from bleaching and dyeing of hair  
 PA Thera-Chemie Chemisch-Therapeutische G.m.b.H.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI DE 1174453  
 GB 990660  
 BE 644474  
 DE 1202441  
 FR 1393604  
 US 3202579 1965  
 IT \*\*\*2809-21-4 4712-06-5 4712-07-6 4712-08-7 31182-41-9

L60 ANSWER 10 OF 10 CAOLD COPYRIGHT 2005 ACS on STN  
 AN CA62:4225g CAOLD  
 TI detergency composition  
 AU Diehl, Francis L.  
 DT Patent  
 TI detergents  
 PA Procter & Gamble Co.  
 DT Patent  
 PATENT NO. KIND DATE  
 -----  
 PI US 3159581 1964  
 BE 651634  
 BE 655988  
 FR 1439824  
 IT 2281-11-0 2666-14-0

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

6.83

558.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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0.00

-35.04

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